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TUBERCULIN AND VACCINE

IN

TUBERCULAR AFFECTIONS

A Practical Guide for the Utilization of the Immune Response in General Practice

BY

ELLIS BONIME, M. D.

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1917

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To the memory of my
MOTHER,
whose sacrifices have shaped my career,
and to
Prof. JOHN ALLEN WYETH, M.D., LL.D.,
who has given me the opportunities that made my
experiences possible,
this work is gratefully dedicated by the Author.

46349

FOREWORD

By JOHN ALLEN WYETH, M. D., LL. D.

Having demonstrated to my complete satisfaction that the persistent and carefully adjusted injection of tuberculin will cause to disappear lymphatic glands enlarged with the inflammatory products of bacilli of tuberculosis, I undertook to establish a clinic in connection with my department of general surgery at the New York Polyclinic Medical School and Hospital, at which these cases could be treated. Dr. Ellis Bonime was placed in full charge of this clinic. His careful technique and conscientious study of each of these numerous subjects who presented themselves for treatment gave a final confirmation to the results of our preliminary work. As will be shown in the text of this volume, the beneficial effects of Koch's tuberculin are now also demonstrated in bone and skin tuberculosis, and the earliest stages of pulmonic involvement.

To this department has been added the treatment of various infections by the use of vaccines and sera, a branch of surgical therapeutics as yet not as insistently taught or as widely practiced as our experience would seem to justify.

JOHN A. WYETH.

PREFACE.

There is, perhaps, no therapeutic agent which has so checkered a history as tuberculin. Every medical man is acquainted with the story of its rise and of its sudden fall; of the prejudices and vicissitudes that have beset its career. However, we believe that the days for defending and apologizing are past, and that every physician who has given the subject any serious thought is convinced that in tuberculin we have the medium through which tuberculosis is destined to be conquered. However, to get any adequate control of this plague, we require a method for the use of tuberculin which will enable the general practitioner to handle it safely. Once the general practitioner is able to cope successfully with tuberculosis by means of tuberculin, the public will gain faith in tuberculin. We have come to realize that the education of the public is quite as important as proper treatment. The idea that the climatic treatment of tuberculosis is the only one known, and thus means banishment from home and occupation, has occasioned a dread of the disease which has created a fear of diagnosis rather than a rush for early treatment. There is no better way of educating the public to come for early treatment than to have a method of treatment in the hands of the general practitioner which will make him able and willing to take the responsibility for treatment instead of shifting it by sending his patients away.

The need of such a method struck me in the course of my work in surgery. I soon noticed, as most surgeons do, the futility of surgery in tubercular conditions. As I had a large and successful experience in the use of the immune response in vaccine therapy in all forms of surgical infections, I could not help thinking that there must be some way of utilizing the immune response in tubercular conditions, especially where surgery so often proves hopeless, and where

other forms of treatment would be so welcome. Thus it was, that when Dr. John D. Murphy of Chicago made his announcement that over a period of two years he had been able to avoid operations on cervical adenitis by the use of tuberculin, I began to use tuberculin in this condition, with pronounced success. As my experience with the use of tuberculin grew, I became more and more convinced as to the efficacy of the artificially induced immune response in tubercular conditions. As I went further into the literature on the subject, and observed the physiological action of tuberculin, I came to realize that the immuno-mechanism in tuberculosis was exactly the same as in any other infection, except that the hypersusceptibility and the production of substances during the immune response was responsible for the dangerous element in the improper use of tuberculin. I observed that the hesitation on the part of the profession to use tuberculin was due to the necessity of judging the patient's degree of hypersusceptibility.

Working along these lines, I finally evolved a system of dosage which eliminates the necessity for judging the hypersusceptibility of the individual, and controls, to a very great extent, the degree of constitutional reaction. My method has been tried out for five years at the New York Polyclinic Hospital, at the Newark Home for Crippled Children, in an extensive private practice, and in several years' experience of a number of my colleagues, who have been kind enough to keep me constantly in touch with their work. It is at the request of these, and of the physicians who come to the Polyclinic Hospital for short courses in medicine, that I have set down the results of my experiences in written form.

This volume will be as short and simple as possible, and will avoid all complicated theories and technicalities. Its aim is two-fold: It seeks first to unfold a method that will attract the general practitioner. I hope, in this way, to help in extending the field of tuberculin therapy far beyond the narrow scope of the specialists,—as there cannot possibly

be enough specialists to reach the majority of sufferers from tuberculosis. My other aim is to reach those patients who have to continue their daily work while under treatment. We know that these are by far the vast majority and that they are the greatest menace in the spread of the disease. In short, I aim at an ambulatory treatment simple enough to reach physicians in every nook and corner, even where the best facilities are not at hand.

I wish to express my appreciation of the works of those authors who have written so fully and convincingly on tuberculosis and tuberculin for what they have done to make my experience possible. As my book is merely a practical guide to the use of the immune response in tuberculosis I could not at every point tell whether my idea arises from my own experience or from the reading of the literature on this subject, and I did not interrupt my work to make the distinction. So that if I failed to make frequent mention of those authorities in my work, it is not from lack of appreciation or from a desire to appear altogether original.

To Doctor Charles Gottlieb for the excellent radiographs; to Doctor Sidney Twinch for the material at the Newark Home for Crippled Children; and to my associates at the New York Polyclinic Medical School and Hospital for their assistance, I am greatly indebted.

ELLIS BONIME.

New York, *August, 1917.*

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Part I

Chapter I

INTRODUCTION

Excepting instances of the immunity which is natural or hereditary, and the passive immunity where the infection was in some other animal, all immunity is the result of *infection* which stimulated the body cells to the formation of specific antibodies. The infection may either be caused by living bacteria, virulent or avirulent, or to a milder degree by dead bacteria.

The word "immunity," as generally understood, means a state of the organism as resisting a special invasion, but we must include the mechanism by which this state is acquired in its broader meaning. When such an invasion occurs, either by the micro-organism or by a physical or chemical cause, the normal physiological processes of the body are interfered with and physical and chemical changes immediately take place in the organism to counteract it; and when this counteraction is accomplished, changes again take place which gradually reinstate the normal processes.

The defensive processes, plus the natural tendency to return to normal, are included in the mechanism of immunity, so that, whether toxic substances or bacterial substances have formed the abnormal state, the gradual return to normal is the immunity acquired, whether it be a toxic immunity or a bacterial immunity.

In the case of infections, we may have a bacterial immunity to deal with—that is, an immunity against the direct action of the bacteria; or, we may have a toxic immunity to deal with—that is, the acquirement of immunity against toxic substances which the bacteria liberate either through their metabolism or through their death; or we may have a combination of the two—that is, we may have an invading organism which not only does harm by its

Part I

Chapter I

INTRODUCTION

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Immunity is always the result of infection.

The word "immunity," as generally understood, means a state of the organism as resisting a special invasion, but we must include the mechanism by which this state is acquired in its broader meaning. When such an invasion occurs, either by the micro-organism or by a physical or chemical cause, the normal physiological processes of the body are interfered with and physical and chemical changes immediately take place in the organism to counteract it; and when this counteraction is accomplished, changes again take place which gradually reinstate the normal processes.

Immunity embraces in its term all process going into the establishment of the state of resistance to the particular infection.

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The immunity may be against the organisms or its toxins or both.

multiplication and extension in the tissues, but may also produce toxic substances which in themselves form protein poisons, doing damage to the organism.

It is in this latter form that treatment seems most difficult, as the established use of vaccines, while active against the organism, fails to produce any results against the toxicity. On the other hand, the use of antitoxins, while neutralizing this toxic substance, still allows the bacteria to multiply and produce more toxicity and direct damage by their presence.

Where the two exist treatment is complicated.

There are two ways in which the organism can acquire immunity. One way is by the natural physiological process in the organism, whether set in motion by the organism directly, or whether stimulated by outside agencies. This is called active immunity. However, the discovery was made that the sera of immunized animals retained the immune substances which we are able to transfer to the sera of other animals, thus merely placing immunity into the circulation without the necessity on the part of the recipient to form his own immune substances. This was called passive immunity.

Active immunity

and

passive immunity.

It might be well at this point to bring out the fact that one form of immunity does not preclude the other in the same organism against the same infection. We can stimulate the mechanism of the immunity in a given individual by certain substances and find this stimulation either too slow or insufficient and so use a passive immunizer at the same time.

A combination of the two advisable in suitable cases.

The Mechanism of Immunity

Since the protective mechanism of the host is specific against each organism, we can easily see how extremely complicated and for the most part theoretical our present knowledge of the subject still remains.

The protective mechanism of the host consists of two elements;

However, the two most important methods of protection stand out very prominently. The first and most far-reaching is the mechanism of phagocytosis with the production of substances which render the invader amenable to phagocytic action.

the Phagocytes

and

the Antibodies.

The second protective process deals with the formation of substances in the blood stream and in the body sera that act directly on the invader in various ways, to destroy or neutralize the poisons of the invader.

The phagocytes and the opsonins which make their action possible.

Taking up the subject of phagocytosis in detail, we find that in order that it prove effective at all, substances must form which combine with the invader to render it absolutely susceptible to phagocytic action. These substances we call opsonins.

These opsonins are negative to each invader and the amount of protection they give the host is in direct proportion to its quantitative existence at the time of invasion. This fact has brought out the subject of opsonic index.

Determination of amount of protection.

Wright has found that the amount of opsonins present in each individual at the time of invasion can be determined; thus, a measure for the amount of protection on the part of the host is at hand. By this measure we are able to determine at any given moment during an invasion, whether the host or the invader has the better of the combat; and it has been undertaken to constantly measure this protection in order to determine the period for rendering outside assistance to the host.

Further work in vaccine therapy has shown that clinical symptoms are sufficient to indicate both the necessity and the intervals for outside interference, making this tedious and highly specialized process of opsonic index determination unnecessary. This is rather fortunate; for, if the treatment with vaccines depended on the determination of the opsonic index, vaccine therapy would have died out completely, or smouldered in the hands of the few.

Opsonic index unnecessary.

Opsonins. There are two conditions absolutely necessary for opsonins to play an effective part in the course of the infection. First, the bacterial invader must be susceptible to opsonic action, and secondly leucocytes, capable of active phagocytic action upon the opsonized bacteria, must be present.

Conditions for opsonic effectiveness.

The number of staphylococci taken up by 100 leucocytes

in a mixture of leucocytes, staphylococci and serum of the patients suffering from furunculosis may be 200. In a smaller mixture of normal serum, under the same conditions, 100 leucocytes may contain 400 staphylococci.

Method of opsonic index determination which proved that small doses of vaccine are best.

Wright found from repeated determinations of the opsonic index that a curve may be plotted which has the general characteristics of other antibodies. The curve may be modified by the inoculation of small amounts of culture of the organism causing the infection. The course of the curve depends on the amount and toxicity of the dose; thus small doses tend to raise the curve. A larger inoculation causes first a depression of the curve below normal (negative phase) and then increases it to a point considerably higher than before (positive phase). If the amount of inoculation is still larger, the negative phase is more marked and of abnormal duration; and may or may not be followed by a positive phase depending upon the amount of excess dosage. The aim of small doses of vaccine, such as would give the maximum dose of opsonic response and the necessity of giving doses at sufficient intervals of time to allow of the development of the maximum reaction from previous inoculation, were repeatedly emphasized by Wright.

Antibodies. In dealing with the second form of protection, in which the substances act directly on the invading organism, we have three distinct forms:

In the immune response there is a production of substances acting directly on the invader.

In the first place, we have substances which tend to paralyze the activity of the invading organism. These substances are known as precipitins and agglutinins.

Second, we have substances combining chemically with the bacteria, causing them to disintegrate. This class of antibodies is known as lysins.

Third, we have substances neutralizing the toxins set free by the bacteria, the substances being designated as antitoxins.

Vaughn and others have shown that if bacteria are digested by chemical means or by treatment with the bacteriological serum, that the toxicity of the suspension is

enormously increased. The inoculation of such a suspension in animals was observed to produce highly toxic symptoms.

Thus, the host may produce a digestive substance as a part of the defensive mechanism,—that is, for the digestion of the bacteria which might produce a very highly toxic combination and which, in its absorption, may seriously injure the host; or, it may cause a local proteolysis of the host's own tissues. Or, the defensive substances (antibodies) produced by the immune response, in combining chemically with the invading organisms (bacteria) may form proteins which are highly toxic to the host.

The end-product of the union of antibody with the invader may be toxic to the individual who is hypersensitive to such substances.

Proteins derived from the action of antibodies upon bacteria may become highly toxic to the host if the host possesses a hypersusceptibility (idiosyncrasy) to these proteins. "Anaphylaxis" is the term applied to the syndrome complex produced by the action of these proteins in hypersensitive individuals; while "allergy" is the term applied to the state of hypersusceptibility produced in an animal, making the production of "anaphylaxis" possible.

The most prominent example of "allergy" exists in tubercular individuals. The infection with the tubercle bacillus is almost universal; but a prompt immune response puts an end to its activity early in life.

However, those individuals possessing or acquiring idiosyncrasy or hypersusceptibility to the proteins produced during the immune response, are subject to a more successful invasion by the tubercle bacilli. For, should an invasion occur,—whether it be by new bacteria or an extension from an old focus, the consequent immune response giving rise to the protein to which the individual is susceptible, will produce a toxic or an anaphylactic effect. This effect, when brought about by an artificial immune response, is better known as "the constitutional reaction." Such a constitutional effect momentarily lowers the resistance of the individual to the invader,—in this case the tubercle bacillus; and so allows of its multiplication and extension into the tissues.

Hypersusceptibility is responsible for the development of tuberculosis.

Whereas, in most of the common infections to which the

The vicious cycle in tubercular affections: The protective response produces toxic protein which allows of extension of the disease.

human race is subject, we aim to obtain a maximum amount of immune response,—in the infection with the tubercle bacillus its severity depends upon the greater immune response. The vicious cycle in tuberculosis is thus made plain. The only means of defense against tubercle bacilli is the immune response; but, owing to the presence of hypersusceptibility, the proteins produced by the immune response poison the individual, allowing of a further extension of the disease. Thus, a vigorous immune response which is curative in other diseases, would tend, in tuberculosis, to produce the active or hasty form of the disease, and the more gradual immune response tends towards the chronicity of the process.

The vicious cycle is responsible for the neglect of tuberculin.

So it has come to pass, that, although no one any longer denies that tuberculin is capable of eliciting an immune response, with an easily demonstrable hyperemia in the diseased tissues, it has been abandoned and even condemned in the treatment of tuberculosis.

Fortunately, there is an increasing number among the profession who have learned that we may acquire a tolerance to a protein poison, and overcome the individual hypersusceptibility, if we produce a slowly increased amount of tolerance by means of a gradual, artificially stimulated, immune response, with the degree of individual hypersusceptibility as an index.

The aim of this book.

The principal aim of this book is to emphasize the necessity of overcoming hypersusceptibility and to advocate the utilization of the immune response in tuberculosis, and to do this by a method sufficiently simple to become practical in the hands of the general practitioner. For it is the general practitioner alone who is able to reach the great numbers of sufferers, and to reach them in the *earliest* stages of the disease. Incidentally, lest our successes prove often useless to the afflicted, I have added, in some detail, methods by which we may remove, or at least modify the *results* of the tubercular affection, obtained *before* the patients presented themselves for treatment,—I am referring to the part under "Special Treatment."

Chapter II

THE NATURE OF TUBERCULINS

The specific remedies for tubercular affections have the same aim as products aiming to produce immunity in all other affections; that is, active immunity and passive immunity. We are mainly concerned with the former. The passive form consists of products cropping up here and there, and aiming at a more direct attack against the scourge, by producing passive immunity.

Tuberculins are modified vaccines.

The passive method of immunity in tuberculosis is thus far in the experimental stage and nothing brought forward, up to this time, gives any promise of antitoxic value. However, we should bear in mind the prevalence of the disease, keeping our minds open to conviction, taking account of every product that may be brought forward through scientific research, in order not to overlook, by too hasty judgment, that remedy, which through the induction of passive immunity, can alone solve the world-wide problem involved. We must not allow ourselves to forget that only with a passive immunizer can we do away with the hypersensitiveness in tubercular subjects with one stroke, and either cure the patient with it alone, or augment the treatment with an active immunizer, such as we now use, without the fear of reaction, producing the same results as we are now obtaining with vaccine in other infections. The following are the three most important antitoxins, or antitoxic sera that have been brought out, and which have up to this time gained the widest publicity:

Antitoxins for tubercular affections have so far not proved effective. However, we must not allow preconceived prejudice to retard the progress of research.

Maragleano's Serum.
Marmorek's Antituberculosis Serum.
Hoechst's Tuberculosis Serum.

Three of the most important antitoxic sera brought out so far.

Each of these, and several of the others which we need not mention here, have raised the hopes of their particular inves-

tigators, but as yet, no passive immunizer has been discovered which can be recommended for general use.

Of the active immunizers, with which we are here concerned, we have the three chief forms as exemplified by Koch's original work and which still represent the basis of all other forms and modifications subsequently produced by others. These products consist of three principal varieties: (1) the soluble secretions of the tubercle bacilli, (2) the bacterial bodies alone, and (3) a mixture of the two. All other preparations, whether derived by Koch himself or by others, merely depend on the method of preparation or concentration, or upon the method of sterilization which takes into account the variations in the extraneous substance, going into the solution from the culture media.

There are three main variations in tuberculins.

Type 1, or Tubercular Filtrates

Koch's OT, AT (alt Tuberkulin) or T, is the most familiar and best example of this type. Its method of preparation is as follows:

Old Tuberculin OT or T.

> Pure cultures of tubercle bacilli are grown from four to six weeks on a 5% glycerine-broth. This is sterilized with the culture fluid by heating for one hour in steam. This is filtered, removing the tubercle bacilli from the liquid, which is now concentrated to one-tenth its bulk in a low temperature oven.

It thus consists mainly of the soluable secretions of the tubercle bacilli, plus a small amount of endotoxin, which is extracted from the tubercle bacilli bodies during the hour of steam sterilization, owing to the presence of alkali and glycerine in the medium.

TOA (Tuberkulin obers alt) is the same as OT, except that it is not concentrated to one-tenth its bulk. When used, it is merely taken in ten times the strength as OT,—using a No. 4 dilution where No. 5 of OT would be used—and so on throughout the dilutions. Its advantage over OT,

Tuberkulin obers alt TOA.

if any, consists only in having to make one dilution less at the beginning of the treatment, but has its great disadvantage at the conclusion of treatment, when a full c.c. and then 2 c.c. of the pure TOA would have to be administered. It is, however, a favorite in some parts of Europe, especially in Switzerland.

AF (albumose-free Tuberculin) is the same as OT, except that the bacilli are grown in an albumose-free medium. It is claimed that it has the advantage of producing less fever during a reaction by the removal of the albumose, which is one of the factors in producing fever. It would, therefore, be well suited for a case with extreme hypersusceptibility, at the beginning of treatment. However, it is extremely difficult to get a constant product, disastrous results having occurred during treatment by a variation in its strength. And it is doubtful whether the quantity of albumose, during treatment, is a factor at all in the production of the constitutional reaction and so, it is best to leave these more difficult products until such a time, when our experience will allow of experimentation.

Albumose-free tuberculin AF.

Type 2, or Bacillary Bodies

The dry tubercle bacilli in a watery emulsion were first used, but found to be impracticable, because the bacillary bodies proved to be non-absorbable in the tissues, and soon formed localized abscesses. Pulverization of the dried bacillary bodies was found necessary, and so the best example of this type was produced by Koch,—i.e. BE or bacillary emulsion.

Bacillus Emulsion BE.

> The tubercle bacilli are removed from the culture medium after sufficient growth, carefully washed, dried and then pulverized. An emulsion is made, by adding one part of pulverized tubercle bacilli, to a hundred parts of a solution composed of equal parts of water and glycerine. This is tested for the presence of living tubercle bacilli, and when found sterile, is ready to be used.

Tubercular Residue or New Tuberculin TR and Tubercular Obers TO.

TR and TO (Tubercular Residue or New Tuberculin and Tubercular Obers) are both derived during the process of emulsifying the BE. The pulverized tubercle bacilli are shaken in the water and allowed to stand until they fall in a sediment. The water is decanted from the top and used as a tuberculin, which is designated as TO. The sediment is emulsified with equal parts water and glycerine in the same manner as BE, and is designated as TR or new tuberculin. Both of these were found extremely inconstant in strength and were soon abandoned.

Sensitized BE SBE or "Tuberkulose-Sero-Vakzin" Farbwerke-Hoechst.

SBE or sensitized BE, or as manufactured by the Hoechst Farbwerke, under the name of "Tuberkulose-Sero-Vakzin," is an attempt to remove the toxic principle of the tubercle bacilli by a specific amboceptor (Antituberculin) by allowing the pulverized or whole tubercle bacilli to remain in contact with a tubercular serum. Striking results have been obtained with this sensitized BE, especially in animal experiments, but it is found that this tuberculin is much more active than any of the others, requiring a sixth or even seventh dilution at the beginning of treatment. Besides the drawback of being much stronger in its effect upon the organism, it is not stable, becoming stronger as it grows older; and it is also very expensive.

Type 3, or Type 1 and 2 Combined

Tuberculol Landsmann a good example of types 1 and 2 combined.

The best example of this type is Tuberculol Landsmann. This is prepared by making a BE and adding this to the filtrate which has been concentrated in vacuo as far as possible. It now undergoes a process of filtration through porcelain candles, and after the addition of phenol to a five per cent. strength, it is diluted until 1 c.c. is a lethal dose to a guinea-pig weighing 250 grm. A more detailed description of the method of preparation may be found—

Landsmann. Zentralblatt für Bakteriologie, Bd. xxvii, 1900.

Hygienische Rundschau, 1898 Nr. 10 u. 1900, Nr. 8.

This tuberculin has the advantage of being absolutely constant in its amount of tuberculin reactivity, as every sample is tested to a given lethal strength. It is, however, highly toxic and very difficult to handle in the beginning of treatment. If used at all, it should be resorted to after a high degree of tolerance has been acquired through the use of OT. In the conclusion of treatment, it is to be highly recommended together with the suggestion of Landsmann, that the final dose should be repeated at constantly increasing intervals for a considerable period of time in order to maintain a maximum amount of tolerance acquired through its use.

The mixture of OT and BE by Beraneck TBk and others.

Wolff-Eisner directly mixed OT and TR. Klebs and Beraneck (TBk) have made similar mixtures. A whole series of preparations have been made by Spengler, mixing the OT and BE in different proportions intended for different grades of hypersusceptibility. Gabrilowitsch made his "Endotin" claiming to have removed the toxic substances from tuberculin, in order to prevent the constitutional febrile reaction, but all these merely represent tuberculins made weaker, for it is the amount of immune response, and not the toxic substances in the tuberculin, which is responsible for the febrile reaction.

In the resumé of the principles involved in the various forms of tuberculin, my aim has been to allow of a glimpse into their differences, in order to simplify the matter and remove the idea which total ignorance of these various products might bring about;—i.e., the feeling that there may be something still better than what we are already using, so that we shall not be tempted to try a host of different preparations without having given any one a fair trial. As I have said before, we can do far more with a tuberculin that may not be the best, but with which we have a long experience, than we can with the best products and with constant change.

Chapter III

CHOICE OF TUBERCULIN

From innumerable investigations and from reports from different clinics, it is now established that Old Tuberculin is distinct from other tuberculins, in that it possesses that element which brings about the maximum amount of tolerance to protein poison and also produces a maximum amount of focal reaction or hyperemia.

This is because OT does not contain the bacillary bodies. Any tuberculin that contains the bacillary bodies, seems to bring about a greater immunity against the tubercle bacillus. It thus produces more antibodies, and causes disintegration of a larger number of tubercle bacilli. Since the protein poison comes from the tubercle bacilli thus killed, it is comprehensible that too great an amount of poison is elaborated by any tuberculin containing the bacillary bodies, making it difficult to gain tolerance to the bacillary poison, and making it extremely liable to severe and dangerous reactions.

OT is best for the production of focal hyperemia.

Old Tuberculin contains a minimum amount of substance stimulating the formation of antibodies. Hence, it can be safely used, because we can more easily control the amount of antibodies and the number of tubercle bacilli killed, and in that way we can control the amount of poison these lysinized tubercle bacilli form.

OT has a relatively small amount of substance stimulating antibody formation, therefore is more easily controlled.

We must not lose sight of the fact that for a cure, to be complete, bacillary immunity must be gained as well as tolerance. Consequently, the bacillary bodies are of great value in this connection after OT has been used to the optimum dose; a dose sufficiently large to establish the fact that hypersusceptibility has been removed.

Any emulsion of tubercle bacilli can act as a tubercular vaccine when hypersusceptibility is removed.

It follows that the ideal choice of tuberculin would be to use OT until the maximum dose is reached, at which point the patient shall have acquired complete toxic immunity and in a large percentage of cases complete healing.

Should the necessity of further treatment be indicated, the ideal situation is present for the use of a bacillary emulsion. The toxic immunity need not be reckoned with any further and bacterial immunity can now be established in the same manner, as with any vaccine.

Dilutions

The usual method of making dilution too complicated for every-day use.

As regards the making of dilutions, as simple as the matter may seem, a great deal of confusion is produced in the minds of those who set out to use tuberculin. This confusion is caused not only by difference in methods expounded, but also by the standard of measures used in naming the quantities of tuberculin.

There should be a universal standard of measurement for tuberculins.

Thus, some authorities measure by weight, others by volume. Now, the former requires a knowledge of the amount of the solid substance in the specific tuberculin used. This knowledge is difficult to obtain in a great many instances and very often varies according to the different authorities. The volume of the tuberculin, on the other hand, always remains the same, and should therefore be the standard of measure in making dilutions.

Make all the dilutions up to the required one instead of attempting to make the higher one direct.

Again, in making dilutions in multiples of ten, one easily reaches the highest dilutions, such as 1 in a million, or 1 in ten-million, without the least difficulty. This method is certainly less difficult and infinitely more accurate than attempting to make the dilution which one requires for use directly.

The use of a one c.c. tuberculin syringe, the same as is used in treatment is best and simplest for dilutions.

Again, the advice given for the use of various measuring glasses, pipettes, graduate cylinders, etc., adds to the size of the mountain in the imagination of the beginner, when only a mole hill is in question. Since, in order to practice accuracy in tuberculin treatment, we must use a finely subdivided tuberculin syringe, why not use the same syringe in making dilutions and thus simplify the whole process? A good tuberculin syringe should consist of all glass, or an accurately fitted metal piston in a glass barrel holding

one c.c. divided into tenths and each tenth subdivided into five or ten parts. Each division therefore holds 0.1 c.c., and each subdivision holds 0.02 c.c. or 0.01 c.c.

½ per cent carbolic in normal saline is best as diluent.

The diluent used in making the dilutions is a half of one per cent. carbolic in normal saline (i.e., one drachm of a 5% carbolic solution added to 9 drachms of sterile normal saline placed in a sterile bottle). This may be used until the appearance of a fungus, when fresh diluent should be made.

FIG. 1.—Tuberculin all-glass syringe.

FIG. 2.—Tuberculine record syringe.

Directions for Making Dilutions

Five wide mouthed bottles holding about a dram each should be numbered 1, 2, 3, 4, 5. (See Fig. 0.)

Draw into a tuberculin syringe 0.9 c.c. of the diluent followed by 0.1 c.c. of the tuberculin. This makes the first dilution. Put this into bottle marked 1.

Draw in 0.9 c.c. diluent followed by 0.1 c.c. from bottle 1. This makes dilution 2 which should be placed in bottle labeled 2.

Draw in 0.9 c.c. of the diluent followed by 0.1 c.c from bottle 2. This makes dilution 3 which is put into bottle labeled 3.

Draw in 0.9 c.c. of diluent followed by 0.1 c.c. from bottle 3. This makes dilution 4 which is placed in bottle 4.

Draw in 0.9 c.c. diluent followed by 0.1 c.c. from bottle 4. This makes dilution 5 and is put into bottle labeled 5.

Special stress is laid on the drawing of *diluent* into the syringe first, followed by the tuberculin or its various dilutions. There are two good reasons for this:

First: The first division of the syringe is not reliable and varies with the size of the needle or the shoulder of the syringe. Thus, measurement of the tuberculin will not be accurate.

Second: In expelling the mixture into its respective numbered receptacle, the tuberculin leaves the syringe first, followed by the diluent, so that if any remains in the needle or shoulder of the syringe, it will be diluting fluid, and no tuberculin will be lost. This will also obviate the necessity of rinsing the syringe after each dilution.

Dilution	*Strength of Dilution*	*Pure Tuberculin in each c.c. of Dilution*
No. 1 contains 1 in	10 or 0.1 c.c.	or 100 c.mm
No. 2 contains 1 in	100 or 0.01 c.c.	or 10 c.mm
No. 3 contains 1 in	1,000 or 0.001 c.c.	or 1 c.mm
No. 4 contains 1 in	10,000 or 0.0001 c.c.	or 0.1 c.mm
No. 5 contains 1 in	100,000 or 0.00001 c.c.	or 0.01 c.mm

Stability of Dilutions

A diversity of opinion seems to exist regarding the stability of the various dilutions. To determine exactly the length of time that each dilution would remain active, would not be at all worth while. It would involve a great sacrifice of time and energy, requiring a mass of laboratory tests and animal experiments, with results that would be practically of no scientific value. The only value would be from an economic standpoint; and this is a very insufficient reason for the waste of time and effort, as the cost of tuberculin, when made up in dilutions, is insignificant. Besides, as is made evident by the foregoing methods of making dilutions, there would hardly be a saving of labor for those having to make up the dilutions for treatment.

Dilutions should be made fresh on the day of use.

I take this occasion to condemn the use of prepared

Ready made dilutions should be avoided.

dilutions put up at distant laboratories, and by men who are not in touch with the patients. No one will fail to feel a degree of gratification from the knowledge of tuberculin such as may be derived from the handling of it, and to acquire an exactness that comes with making one's own dilutions. After making these dilutions once or twice the utter simplicity of this method becomes apparent.

NOTE: Solution No. 1, if kept two or three weeks in a dark cool place and if no precipitate forms, will remain stable that length of time. It is well to keep what remains over from No. 1 dilution until just before making the next dilutions. Occasionally there will be an unexpected delay in obtaining the original pure tuberculin and the left over No. 1 can be used in such an emergency.

FIG. 3.—BOTTLES FOR DILUTIONS.—Bottles holding 1 c.c. are sufficient for ordinary office use. As will be noticed above, the author has used empty tuberculin bottles in his office.

FIG. 4.—BOTTLES FOR DILUTIONS.—Bottles holding between 5 c.c. and 10 c.c. are necessary for dispensary, hospital or sanitarium use.

Chapter IV

THE TUBERCULIN REACTION IN DIAGNOSIS

Following the tendency of all things to go in the direction of least resistance, the medical profession has usually tended to avail itself of the easiest way and the nearest elements at hand to help in the diagnosis of disease. With the extended use of tuberculin, this inclination may result in a too ready employment of this agent as a means of diagnosis,—since its ease of application will tempt the diagnostician much more readily than will the routine of physical examination or the examination of sputum, systoscopic examination, catherization of the ureters, Roentgenographic examinations or other means, many of which require the sending of the patients to a distant laboratory, and all of which demand the consumption of valuable time.

The ease of application should not lead to the indiscriminate use of the tuberculin test.

This condition may lead to the abuse of the tuberculous, so let me emphasize at the outset that a tuberculin constitutional reaction heightens the hypersusceptibility of the patient, and so increases the difficulty with tuberculin treatment in proportion to the severity of the constitutional reaction thus brought about. As far as the local tuberculin reactions are concerned, there is no harm in their utilization whenever desired, with the exception of the conjunctival test of which I shall speak under a separate heading. But, in the case of a test which requires a constitutional reaction for its value in diagnosis, tuberculin must be used only as a method of last resort. So long as we have means at hand to establish a diagnosis without tuberculin, so long should we avoid its use. By adhering to this maxim, we shall make use of the constitutional reaction in diagnosis only in the very early stages of the disease, where all other methods of diagnosis have failed, or have failed to produce definite findings. We shall then be applying it in cases where even with a severer constitutional reaction the damage will not be great.

A severe tuberculin reaction will increase the difficulty of tuberculin treatment.

While the local tests are harmless, the constitutional reaction as a test should be utilized as a last resort only.

The ability to recognize the phenomena of the tuberculin reaction will grow with experience, thus constantly increasing the value of tuberculin in diagnosis.

Once the proper place of tuberculin in diagnosis is established, it becomes a valuable asset in our hands; for, by its means we shall be able to discover early processes which have been impossible of discovery without tuberculin, yet which, when discovered are the most amenable to the tuberculin treatment. The more frequently tuberculin is used in diagnosis, and the longer the phenomena connected with the reaction it produces are studied, the greater becomes its value in the diagnosis of tuberculosis and the more devoid of any damage to the patient.

All tuberculin reactions have the infallible quality of detecting the presence or absence of hypersusceptibility.

The tuberculin reaction is essentially a reaction to hypersusceptibility. Whether, as I shall explain further, any one of the methods of the utilization of tuberculin in diagnosis enables us to discover an active lesion or not, it is certain that they all detect hypersusceptibility which means the presence of a tubercular lesion healed or otherwise somewhere in the body, with the possibility constantly present of an extension or reawakening of the process some time in the future. This is why the tuberculin method of detecting individual hypersusceptibility is destined to become the greatest instrument for the ultimate prophylactic treatment against this dread disease, for it will be the means of distinguishing the individuals requiring such prophylaxis from those who are naturally immune to tuberculosis.

hence

Its greatest importance will be recognized when an effective prophylatis will obtain universal application.

There are hundreds of reports in the literature of tuberculin such as those of Binswanger and those from the army recruiting stations in various parts of Europe, all of which leave no room for doubt that all individuals destined to succumb to tuberculosis would be found by means of a tuberculin test to possess hypersusceptibility; whereas the natural immunity exists among those who do not possess such hypersusceptibility.

Indication for Tests

The indications for the use of the tests divide the various tests into two groups. The tests which aim to produce a localized reaction only may be indicated in

any case and may be used as often as desired,—for they leave very little, if any, effect upon the patient. The only exception is the conjunctival test, of which I shall speak later. On the other hand, the indications for the use of the constitutional reaction in making the test should be carefully considered before it is applied. Thus it should be applied only as a last resort method of diagnosis, and only in such a way as will not jeopardize the status of the case with reference to tuberculin treatment, if it should be determined upon.

Special indications need be considered only in the case of the subcutaneous test.

Interpretation of the Tests

Since the object of tuberculin diagnosis is to discover active disease, and since the reaction to tuberculin is a reaction to hypersusceptibility alone, we must take into account other manifestations occurring during the reaction in order to derive the full benefit of the diagnostic value that the various tests possess. In the case of the localized reaction, we can consider them diagnostic of active tuberculosis only in such cases where hypersusceptibility must exist together with the active form of the disease; in other words, in cases where the process had no time to heal. This can be true only in children up to three, perhaps four years of age. The tubercular process when only suspected (thus requiring this test) is bound to be the first process attacking the child, and so the mere presence of hypersusceptibility is sufficient to establish the diagnosis of active tuberculosis. Under these circumstances, any test bringing about a local reaction alone is sufficient. But, when dealing with an older individual, where a slight lesion healed and was not noticed previous to the present suspected attack, the detection of hypersusceptibility is not helpful in the determination of the diagnosis. Fortunately however mild the reaction may be, there always occurs a hyperemia around the lesion during the time of constitutional manifestations of the reactions and thereby renders it valuable in the detection of an active lesion.

Other phenomena occurring during a reaction make it diagnostic of active disease except in very young children where the mere presence of hypersusceptibility is sufficient.

A focal reaction always takes place even with the mildest constitutional reaction.

The focal reaction or the hyperemia can only occur in the tissue which is the seat of active disease, thereby increasing physical signs and symptoms originating in such tissues.

This hyperemia or focal reaction as it is called, produces an increase of the inflammatory process in the lesion, and in that way exaggerates any symptoms or signs which its localization in the body would otherwise produce. Such exaggeration is all that is necessary to remove the doubt that existed with regard to the nature of the condition that made the test necessary. Thus, indefinite physical signs at the apex of the lung will become definite during the constitutional reaction. Râles will become more prominent, dullness more definite, etc. The patient will complain of increased cough and expectoration. During this time the sputum may show tubercle bacilli, whereas before, repeated examinations failed to demonstrate them. Suspected mediastinal glands may make themselves more prominent by a slight swelling that is produced with a focal reaction during the constitutional reaction. Such swelling would produce pressure in the chest, a sensation of fullness behind the sternum and even dyspnea. The hyperemia produced in glands of the neck will render them more tender during the reaction, thus establishing the fact that they are tubercular. Urinary symptoms may be increased and even tubercle bacilli demonstrated in suspected genito-urinary tuberculosis during a constitutional reaction; and so on through the list.

A negative cutaneous test obviates a series of subcutaneous tests.

The fact that the absence of hypersusceptibility excludes a tubercular lesion, might make it advisable to establish the fact of the presence of hypersusceptibility by the simpler local test before the subcutaneous test is resorted to. In that way we might occasionally spare the patient hypodermic injections of tuberculin by ruling out hypersusceptibility.

Dosage

The dose of tuberculin generally advised aims to produce a constitutional reaction in all cases and is

In a constitutional tuberculin test for the diagnosis of tuberculosis, the subcutaneous method is the only one where the consideration of the amount of tuberculin is necessary, as the amount of tuberculin used in the localized test is unimportant. The constitutional reaction varies in severity in

proportion to the amount of tuberculin used, plus the degree of hypersusceptibility present. Most writers on the subject of tuberculin diagnosis advise a dose of tuberculin which experience has shown produces a constitutional effect in all cases where a tubercular process is present. They give consideration to this subject with only one aim in view, and that is, to produce a reaction for diagnostic purposes and take no cognizance at all of a contemplated treatment with tuberculin in case the test establishes a diagnosis of an active lesion. I believe that such an attitude is not to be recommended even without the contemplation of tuberculin treatment; for, if a constant quantity is used for all cases, the constitutional reaction will vary in proportion to the degree of hypersusceptibility in the individual, and if such a quantity is calculated to produce a constitutional reaction in an individual with a small amount of hypersusceptibility, it will be very severe in those who possess a higher degree of hypersusceptibility.

consequently too large for some.

In the latter case, whatever the contemplated treatment may be, the chances for recovery in such an individual have been greatly diminished. Not only does a severe constitutional reaction produce great harm to the afflicted, but helps greatly to increase the prejudice against tuberculin treatment; for, here again the *apparent* fault in the production of the harm is with the tuberculin; whereas the *real* fault lies with the quantity of tuberculin used.

The severe reactions produced during a test have increased the prejudice against tuberculin treatment.

Severe reactions have also helped to produce an array of contra-indications to the tuberculin test which should really be considered as contra-indications to severe tuberculin reactions, and when a limitation is placed on the amount of constitutional reaction for the purpose of diagnosis,—all these contra-indications will lose their purpose.

Contra-indications to the constitutional reaction disappear with the divisional method of dosage.

When a patient presents himself for the diagnosis of tuberculosis, and the importance of establishing a positive or a negative diagnosis is explained, it will be a great exception if such a patient object to two or three or even four

tests, especially when the safety of such a procedure and the danger of the single test method is pointed out.

The quantity of tuberculin used for a diagnostic constitutional reaction should be 10 times the beginning dose advised in the treatment of the same condition.

The amount of tuberculin to be used in a subcutaneous test should be no more than ten times the quantity to be used in such form of tuberculosis as is recommended as the beginning dose in its treatment. (See page 23.) For example: If a pulmonary lesion is suspected and 0.10 c.c. of the fifth dilution is the dose for the beginning of the treatment of pulmonary tuberculosis, 0.10 c.c of the fourth dilution should be the quantity of tuberculin used as a subcutaneous inoculation for the production of a constitutional reaction to establish the diagnosis. If that amount prove insufficient by producing a negative result, the test should be repeated in forty-eight hours and five times the quantity of tuberculin used the first time should now be inoculated; that is, 0.50 c.c. of the fourth dilution. Should this fail, 0.10 c.c. of the third dilution should be used in forty-eight hours, and if that should be negative, 0.50 c.c. of the third dilution used is as a fourth inoculation. As a final test, 0.10 c.c. of the second dilution should be given forty-eight hours later, the last dose being the one recommended usually as the quantity to be used for the test. If, as it very frequently occurs, there is a reaction from the first dose, the temperature rise during such a reaction will not be very marked, with the constitutional symptoms even less marked. But how would such an individual fare with the last dose of tuberculin which is one-hundred times the quantity? Even were the patient to react to the fourth test for the first time, this would be brought about by only one-fifth of the quantity usually recommended, and to inoculate five times the quantity that would suffice to produce a reaction, is sufficient to cause a dangerously severe reaction.

The inoculation should be repeated every 48 hrs.; every subsequent dose should be 5 times greater until 0.10 c.c. of the 2d dilution is reached and when that produces no reaction the test is negative.

Again, it may be argued that where more than one inoculation is made for the production of a reaction, the tolerance gained from the first inoculation may prevent a reaction from the subsequent ones and thus exclude the diagnosis of tuber-

culosis where it might exist with a low degree of hypersusceptibility. Such an occurrence is prevented by making the reinoculations at no greater interval than forty-eight hours. Tuberculin, when given in such increases as recommended for the test, when repeated in forty-eight hours, rather tends to superimpose the effect of one dose upon the other than to gain any tolerance for the patient, for its action does not stop in forty-eight hours. On the other hand, with this method of producing a constitutional reaction for diagnosis, we hardly jeopardize the good effects that might be obtained with tuberculin treatment in the event of a positive diagnosis. Another great advantage that may be derived from such a method of eliciting a constitutional reaction for diagnostic purposes is that this method becomes more or less a measure for the individual hypersusceptibility present, so that if the patient does not react to the first three doses but does to the fourth, we could begin treatment in this case with the third dilution instead of with the fifth and so save a considerable period of time both in arriving at the maximum amount of tolerance and in the total length of time required for the treatment.

The serial test thus becomes a measure of individual hypersusceptibility.

Tables of Dosage for Subcutaneous Tests

Pulmonary

OT	Dilution	No. 4	0.10 c.c.
"	"	No. 4	0.50 c.c.
"	"	No. 3	0.10 c.c.
"	"	No. 3	0.50 c.c.
"	"	No. 2	0.10 c.c.

Bone and Joint Tuberculosis
and
Uro-Genital Tuberculosis

OT	Dilution	No. 3	0.10 c.c.
"	"	No. 3	0.50 c.c.
"	"	No. 2	0.10 c.c.

Glandular Tuberculosis and Lupus

OT Dilution No. 2 0.10 c.c.
" " No. 2 0.50 c.c.
" " No. 1 0.10 c.c.

Contra-indications

The principal contra-indication of the tuberculin test is the possibility of a diagnosis by other means.

There are no contra-indications to the local tuberculin tests, except those mentioned in connection with the conjunctival test. There is, however, an ever present contra-indication to the use of constitutional reaction for diagnosis and that is the *possibility of making a diagnosis by any other means.* It is far better to begin the treatment of doubtful cases and form the conclusion later that the case is not tubercular from the failure of obtaining a reaction during a treatment, than to produce a severe constitutional reaction in a case that is tubercular. Other contra-indications are as follows:

Heart disease is no contra-indication to the milder reaction produced by the above procedure.

Heart disease. Owing to the disturbances in the circulation produced by very severe reactions in isolated instances, heart disease was deemed by some authorities to be a contra-indication to the tuberculin test. This is, however, true only of the very severest forms of heart disease, such as myocarditis or fatty heart and very severe valvular diseases, in which conditions it makes very little difference in practice whether we know that the patient has tuberculosis or not; so these need not be discussed here. The milder reaction obtained by the divisional injection of tuberculin as suggested above will produce no harm whatsoever in the ordinary form of heart disease.

Nephritis is a contra-indication.

Nephritis. Nephritis, we must consider as contra-indicating the subcutaneous test. It is well known that any febrile reaction produces albumen in an individual with healthy kidneys and it is therefore far better to treat a case with tuberculin, although the diagnosis is doubtful, than to run the risk of causing permanent damage to the kidneys, which are already the seat of nephritis, in order

to be sure of diagnosis before treatment. It is well to state right here that a routine urine examination should be made before every subcutaneous test.

Intestinal ulcerations. During convalescence from acute disease such as typhoid, pneumonia, peritonitis, acute appendicitis and gastric ulcer, where a tubercular basis to these ulcerations may be suspected, a constitutional reaction may lead to too great a focal reaction or hyperemia, rendering an increasing peristalsis from any cause liable to set up a fatal hemorrhage. Treatment under such circumstances is not inconvenient for the patient, for the suspicion of tuberculosis presupposes too slow or poor convalescence, thus requiring visits from the physician anyway.

The suspicion of tuberculosis in an ulcerative infectious process in the alimentary canal contra-indicates the constitutional test.

Contagious or infectious diseases preceding less than six months a condition requiring the constitutional reaction for diagnosis, absolutely contra-indicate a subcutaneous tuberculin test, for a hypersusceptibility following contagious diseases in children or any acute infection whether in child or an adult is so marked, that even a carefully applied test may call forth a very severe reaction.

The constitutional reaction is apt to be too severe soon after contagious diseases even by the divisional method.

General miliary tuberculosis. The subcutaneous tuberculin test is contra-indicated where general miliary tuberculosis is suspected.

Epilepsy. The subcutaneous tuberculin test in epilepsy is contra-indicated no matter how long the patient has been free from a seizure in the latter trouble.

General miliary tuberculosis and epilepsy are absolute contra-indications.

Fever. The presence of fever is another contra-indication to the test; as a patient suffering from fever more or less distorts the mechanism of the tuberculin reaction, a foreign injection during fever may merely cause a higher rise. If a patient with a temperature is suspected of tuberculosis, treatment of that patient should be commenced with tuberculin, because as said elsewhere, if the temperature is caused by a tubercular process, tuberculin treatment will soon act as an antipyretic and reduce that temperature. The tuber-

The presence of fever contra-indicates the subcutaneous test.

culin treatment in this instance could do no harm, should the patient turn out to be non-tubercular. If, however, the patient is tubercular, then no time has been lost in applying the tuberculin treatment.

Hemopytsis is so constant an indication of pulmonary tuberculosis that no test is required.

Hemoptysis. Recent hemoptysis in case of suspected lung tuberculosis is a contra-indication to the subcutaneous tuberculin test. The same condition holding true in case of fever holds true in a case following recent hemoptysis. Careful treatment with tuberculin is indicated, and is of great importance to the patients, as all these individuals can be classed under the very beginning stages where tuberculin has its maximum effect. A lung lesion with physical signs so few as to make the diagnosis doubtful, together with the fact that so few conditions other than tuberculosis produce hemoptysis, makes the treatment for these conditions with tuberculin absolutely justifiable. It goes without saying that before beginning treatment of such an individual, the physician must make sure that the bleeding was not from the gums or other chronic conditions in the larynx, pharynx, naso-pharynx and nasal passages.

Determination of the Tuberculin Test

A second application of the cutaneous tests is advisable in order to verify a negative finding.

The local tuberculin test merely determines the presence of hypersusceptibility. It also determines the presence of a previous lesion, except where the individual tested is too young to have had a previous lesion. The negative results, however, are sufficient to exclude the presence of a tubercular lesion, taking it for granted that the tests were properly carried out. In order to be certain, it is advisable in all such instances to repeat the test for the verification of the negative finding. In the case of the subcutaneous test, the determination of the positive finding will rest with the presence of a well defined focal reaction.

The following two reports are but examples of many such investigations with no less striking findings made in

various parts of the world, showing the absolute specificity of tuberculin to the presence of hypersusceptibility and tubercular infection. Incidentally, they emphasize the fact that the constitutional reaction is absolutely safe and is not capable of rendering a closed or healed lesion active, in spite of the assertion of the antagonists of tuberculin that the reaction renders the tubercle bacilli "motile, causing reawakening of the process, spreading the disease beyond its original focus."

Report of Binswanger.

One report is that of Binswanger (Arch. f. Kinderheilk, 1906, Bd. xl, Heft 1-4). Of 261 children whom he injected, 35 reacted. Of these 261 children thus tested, 42 came subsequently to post-mortem examinations, the children having died from various causes. Of these, 16 had reacted positively during the tests and were now all found to be tubercular. Of the remaining 26 who failed to react, 25 were found to be free from a tubercular lesion, only one having any sign of tuberculosis. Even this one did not prove an exception to the negative finding, as the injection was made in the fifth week of its life, when in all probability infection had already taken place, but no tubercular lesion had yet time to form until after the test.

Recruiting army posts report.

Through the reactions in various experiments made at army recruiting stations in different parts of Europe, it was found that the subcutaneous tests were positive in from 30 to 60 per cent. of cases. Upon investigation, it was found that the higher per cent. were found among those coming from areas with known widespread tuberculosis, and that those soldiers coming from less infected areas, showed the smallest percentage of positive test. The two points to be deduced from these findings are: first, the absolute specificity of the tests; second, that in healthy individuals the subcutaneous test is of no greater value than the cutaneous test and the percutaneous test. It merely points to the presence of tubercular infection, which may have existed before and which is cured. One more important point was

determined by these tests as made in great numbers: that at no time has the test in question caused a reawakening of a former lesion, thus emphasizing the findings of a great many authorities, that the subcutaneous test is not harmful to the individual with healed tuberculosis. Hence, we can conclude that the subcutaneous tuberculin test has all the merits of the other tests, plus the great advantage to be gained by measurable doses. The knowledge of the exact quantity absorbed, when figured in relation to the reaction produced, has the great additional advantage of helping to determine the activity and the extent of the tubercular process. Thus, the rapid reaction to small doses, indicates a more active recent disease, whereas slow reaction to repeated increasing doses of tuberculin may point to an older chronic process. The degrees between these two are numerous and have to be determined by careful observation of the patient's history and clinical manifestations before and immediately following the test. It is therefore impossible to lay down schematic rules for the determination of a tuberculin test.

Cutaneous Tests

The cutaneous test of von Pirquet is the most important and most widely used.

Technique of von-Pirquet test.

The technique is very simple; the flexor surface of the forearm is preferred both on account of the absence of hair and the ease with which the findings can be read. The skin is rubbed with ether and scarifications made about two inches apart, three in number and no more than about 1/16 inch in diameter. The scarifications can be made with an ordinary needle, but great care must be taken not to penetrate beyond the epidermis in order not to draw blood. A moment or two after scarification, a slight serous moisture should appear on its surface. The flat end of a toothpick is dipped in pure old tuberculin and rubbed over the two end scarifications, using a separate toothpick for each. A dry toothpick is used in the same manner over the middle scari-

fication so as to produce the same amount of trauma on all three. The scarifications are deemed insufficient if a tiny scab does not form over each in an hour after the procedure.

Bleeding must be avoided in order to prevent absorption of the pure tuberculin; for, however small the quantity, it can still cause a constitutional reaction in a sensitive individual. We must remember that hypersusceptibility might exist to a very high degree in early infection even though the infection may be so mild as to escape recognition, requiring this test for a diagnosis. One ten-thousandth of a cubic centimeter of old tuberculin would give a violent reaction in many early cases of pulmonary tuberculosis, and one ten-thousandth of a cubic centimeter of pure tuberculin is so minute in quantity that a deep scarification would allow of its ready absorption. The middle scarification is the control scarification.

Interpretation. The interpretation can usually be made at the end of forty-eight hours, when the maximum effect is developed. However, the result is often well marked in twenty-four hours and very rarely takes three, five or eight days before full development of the reactions occurs. We have two reactions,—the traumatic reaction and the reaction of hypersusceptibility.

The fully developed reaction should be looked for during the second twenty-four hours.

The traumatic reaction occurs over all three scarifications. It consists of reddening, with a formation of a scab the size of a pinhead, falling off in about twenty-four hours, leaving a pale brown discoloration behind.

The reaction to hypersusceptibility or the positive cutaneous reaction has a latent period of about five hours to several days, but in most cases it develops after twenty-four hours, and reaches its maximum in forty-eight hours. The reaction consists of an exudate and a hyperemia, making itself manifest in a raised reddening, starting from the scarification and increasing outward until it reaches a diameter of about 10 mm. If the reaction is very severe, this might reach 20 mm. or even 30 mm. in extent, with many small

Care should be taken to distinguish a mild reaction from a traumatic reaction.

papules forming around the edge of the reaction. Even a bluish-red areola might appear where the reaction is intense. After forty-eight hours the redness begins to fade, passing over into a very faint violet, leaving a slight pigmentation, which may remain visible for a long period, and finally disappearing with a slight scaling of the skin.

Variations. The variations in this reaction are innumerable, depending in the first place upon the state of hypersusceptibility at the time of the test, the stage of the disease, and the general circulation of the patient. Thus an anemic individual will show a paler papule than one with good circulation; and a well nourished individual will have a larger papule with vesicles better marked than one who is emaciated.

The degrees in the positive von Pirquet vary, but all are diagnostic.

In comparing the test scarification with the control scar, one must allow a certain degree of difference even for a negative result, for the tuberculin contains irritating material, affecting even the tuberculosis free individual. This fact has led von Pirquet to warn the profession against considering a local papule less than 6 mm. in diameter, as a reaction, even though it looked more inflamed than the control scar. In case of doubt, it is advisable to start a new test on the other arm after forty-eight hours. The second test will be decisive; for it is an established fact, that even the local inoculation of tuberculin will increase the hypersensitiveness of a tuberculous individual, and will render the second test more pronounced than the first test. In doubtful first tests, the slight increase in the severity of the second test will be sufficient to decide the question. The increase in the second reaction is far more diagnostic than the ordinary test, for it shows a universal sensitization of the organism with the first test; and it has been frequently shown that tuberculin cannot sensitize an organism perfectly free from tuberculosis.

Negative finding. The negative finding of the cutaneous

a. Well marked reaction.

b. Mild reaction.

Fig. 5.—The Positive Von Pirquet Reaction.

test, especially of the second test, speaks absolutely for the absence of tuberculosis in any form. The following exceptions should be noted: After tuberculin immunity following specific treatment in individuals suffering from general cachexia, and in peculiar skin conditions. In those cases, where in spite of demonstrable tubercular processes this reaction is negative, there are either spent tubercle bacilli, as in fungoid fistulae, or suppurating local conditions, or else the organism has lost its reactive power. This last condition von Pirquet explains as being caused by the absorption of the ergins (the bodies which cause the reaction between the tuberculin and the cells) preventing tubercular allergin, which is responsible for the rapid spread of the disease in those individuals. This phenomenon is explained by von Pirquet in connection with negative results obtained in children suffering with the measles or during the incubation period of scarlet fever.

The negative finding is of the utmost diagnostic value in the exclusion of tubercular infection.

This explanation fits well with the often noticeably rapid spread of an otherwise mild tubercular process, following measles, scarlet fever and other infectious diseases; also during pregnancy. Since these negative findings are based upon the loss of the immune response they occur only in cases of evident tuberculosis and do not lessen the value of the tuberculin test in those cases where the establishment of a diagnosis by the tuberculin test is necessary.

Positive findings. The positive findings in cutaneous tuberculin tests merely point to the fact that tuberculosis exists. It gives no clue as to its location, nor does it prove its clinical existence. This fact should be borne in mind, especially when testing adult patients. A positive well marked reaction should put us on our guard and a thorough search should be made for a tubercular focus. A subcutaneous test to bring about a constitutional reaction seems best indicated under these conditions. The focal manifestations during a constitutional reaction will aid greatly in the localization of an active process. (See page 40.)

The positive finding is of diagnostic value in very young children.

In children up to the fourteenth year, the diagnostic indications of the cutaneous tuberculin test is at the highest degree. In von Pirquet's clinic, where thousands of children have been tested, 97% of tubercular children gave positive reaction or showed naked eye evidence of tuberculosis at autopsy. No case which ever gave a negative result showed any gross or miscroscopic signs of tuberculosis.

Escherich's Needle Tract Reaction

This reaction is practically a local reaction, such as we get in subcutaneous tests. The recommendation is to use 0.20 c.c. of No. 3 dilution in the subcutaneous tissue on the flexor side of the forearm. If the reaction is positive, a red spot appears sharply circumscribed and quite distinct from the red areola that forms around the needle puncture. This begins in about six hours and comes to its height in about forty-eight hours, after which it begins slowly to disappear. Infiltration, edema and great tenderness accompanies this reaction as a rule. When no general reaction occurs and this local reaction is indistinct, the dose may be doubled.

Technique of Escherich's needle tract reaction.

The indications for this test, as well as its positive findings, are the same as for the von Pirquet. Its disadvantage lies in its much greater liability to produce a constitutional reaction. It therefore should not be given preference over the von Pirquet. It should be used only after a doubtful von Pirquet for confirmatory purposes where the technique of the von Pirquet was uncertain and a surer entrance of the tuberculin into the skin is required.

Percutaneous Tuberculin Test of Moro

Technic of the Moro test.

Moro used inunctions of equal parts of Koch's old tuberculin and anhydrous lanolin. He recommends as the site for the inunction, the abdominal wall beneath the ensiform cartilage, or the skin of the chest above the nipple; but considers the use of the forearm as unsuitable for this test. A quan-

tity of the ointment, about the size of a pea, is rubbed for about a minute with the index finger over an area of 5 c.m. in diameter using moderate pressure. A protection for the finger is unnecessary, as the surface of the hand or finger does not react to tuberculin. The inunction area should be exposed to the air for a few minutes and no further attention paid to it. Dressing is unnecessary. The reaction appears both as to time and grades of intensity, in the same manner as with the cutaneous test of von Pirquet. From the mass of literature on the subject, there can be no further doubt that the positive reaction is absolutely specific.

There is no contra-indication to this test, except in pronouncedly scrofulous children. Here a distant cutaneous reaction might occur, causing great discomfort from itching and occasionally seriously affecting for the worse the scrofulous process. It shows a great many less positive reactions in known positive cases than the von Pirquet test and has not the advantage of limited area for its manifestation. The only instance where it might be advantageously used in preference to the von Pirquet, is in a case where the physician does not wish to disclose to the patient the nature of his test, or the fact that he is testing at all. For instance, there are mothers who fear an inoculation of the disease, when the inoculation method is used, leaving the Moro test as the only choice. The modifications of the Moro test, such as Lignieres' and Lautier's are much inferior to the original Moro and cannot be recommended.

Except in isolated instances this test is inferior to the von Pirquet.

Intracutaneous Tuberculin Test

The intracutaneous tuberculin test consists of the injection of a quantity of tuberculin into the skin, and under no circumstances should the injection be deep enough to make it hypodermic. The place chosen should be the thigh, arm or inner side of the forearm. A fold of skin is raised, the needle puncture is made flat in the skin and is pushed parallel with the fold for a very short distance. Solution No. 3

Technic of the intracutaneous test.

of old tuberculin is used and such quantity injected as will raise a white wheal about ⅛ to 3/16 of an inch in diameter. The white wheal disappears in about 20 minutes, and nothing remains visible except perhaps the needle puncture, until the positive reaction sets in, which is in about five to six hours, reaching its maximum within forty-eight hours.

The positive reaction develops during the second 24 hrs. reaching its maximum in 48 hrs.

Commencing with a slight infiltration, appreciable only to touch, the infiltration increases until it reaches about an inch in diameter, surrounded by an inflammatory area, which sometimes reaches in extent to the size of the palm of the hand. In the center of the infiltration appears a reddish, sometimes edematous area, with an erythematous edge. The area may be covered with small red papules; or, when the reaction is severe, actual blistering occurs. After forty-eight hours the infiltration begins to subside, inflammatory symptoms begin to diminish and in a few more days the mark disappears nearly entirely with the scaling of the skin. The hard infiltration may, however, persist for weeks. If the test is negative, only a very slight induration with the faintest brown coloration occurs, disappearing in about two days; and since positive reaction would reach its height by that time, there is no difficulty in recognizing it, even if very mild.

The danger of a constitutional reaction and the great discomfort it often produces, render it inferior to the von Pirquet.

This factor is the favorable feature of the intracutaneous tuberculin test. But Angel's claim that it produces no discomfort is disputed by a great many authorities who have used this test extensively. My own observation found that the positive reaction produces great discomfort with inability to use the arm for several days; also a definite constitutional effect has often appeared, including focal reaction, such as enlargement of tubercular glands of the neck. The general effect of the intracutaneous test is the same as the cutaneous one, with the added disadvantage of greater intensity of its action. However, it can be used with advantage, where the cutaneous test is negative, on account of the control of the quantity of tuberculin used in

the test; thus, Angel recommends the use of 1:5000 dilution first, 1:1000, 1:100 and finally 1:10. This test is also of value where the subcutaneous test is contra-indicated and the cutaneous test has proved negative. However, the sphere of this test cannot be extended beyond that of the cutaneous test, and seems to be limited to early childhood, rendering its fields of usefulness extremely small.

Conjunctival Tuberculin Test

This test was discovered by Calmette and Wolff-Eisner, as a modification of the von Pirquet test, and was reported under the names of "ophthalmic reactions" and "conjunctival reactions." The latter name is more appropriate, as the reaction occurs in the conjunctiva only. Special tuberculins were at first deemed necessary; but according to Bandelier and Roepke and others, the original Koch's old tuberculin is the best. It obviates the difficulty of obtaining the special kind and is a great deal less expensive (95% alcohol precipitate of tuberculin dried and sold in small ampules, a watery solution to be made at the time of use). The technique is very simple. An ordinary dropper can be used, a single drop of one to four per cent. of old tuberculin in adults, and a half to one per cent. in children. The drop is placed in the conjunctival sack, care being taken that the end of the dropper does not touch the sack and cause a flow of tears, or movements of the lids that may expel the tuberculin. The tuberculin is now kept a minute or two in the closed eye and no further attention necessary; no bandage or eye protection is required.

Technic of the conjunctival test.

The reaction begins in from five to six hours and usually comes to its height in about twenty-four hours, remaining visible for several days afterwards. The reaction grades from a reddening of the conjunctiva, which can only be seen on everting the lid and comparing it with the other side, to a reddening of the entire conjunctiva visible from a distance. In severe cases, swelling, much fibrinous or purulent secre-

tion, and even echymosis may appear. These tests may be repeated two, three and four times and it is advisable to begin with a much weaker solution than is usually used in order to avoid the severer form of the conjunctival reaction in hypersensitive individuals. Begin with the 1% solution and increase to 2, 3 and 4% in the subsequent tests. It is also advisable to use each eye alternately, as the severe forms of reaction occur in patients where an overlooked positive reaction in a conjunctiva has increased the hypersensitiveness of that conjunctiva and caused the reaction from the second installation to be very severe.

The specificity of the test is beyond doubt as true of the conjunctival test, as it is of the cutaneous or intracutaneous test. However, this test cannot be recommended, for not only is it often dangerous, causing severe damage to the eye, but its negative finding is not reliable, as over fifty per cent. of early active tuberculosis have shown negative reactions in the hands of many investigators. Special warning should be taken against the use of tuberculin in a conjunctiva that has been the seat of a positive reaction, no matter what length of time intervened. This warning also applies to the use of a conjunctival test following a cutaneous or subcutaneous test, before the hypersusceptibility awakened by these tests has entirely subsided. Under no circumstances should a cutaneous or subcutaneous test be made before a conjunctival test has entirely subsided, as the increased susceptibility produced by the cutaneous and subcutaneous tests might reawaken the conjunctival reaction and cause a very severe reaction in the conjunctiva.

This test should not be used as even its negative finding has no diagnostic value. It is also dangerous to the eye.

It can thus be seen how a positive conjunctival test may interfere with the necessary therapeutic tuberculin inoculations. Once the conjunctiva has been rendered sensitive, it may severely react after each dose of tuberculin even though the quantity may not be sufficient to cause a constitutional reaction. I have now under my care a little girl nine

Hypersusceptibility may remain in the conjunctiva after

years of age, who has been treated for tubercular adenitis for over a year without marked success. A conjunctival test was made in order to determine the nature of the glandular involvement and proving positive was sent to me for tuberculin treatment. At present I have the greatest difficulty in gauging the dose of tuberculin, as the slightest approach to maximum tolerance causes a severe conjunctivitis. Above all, we must take special heed that every possible eye disease be excluded before a conjunctival test is undertaken.

a test causing recurrence of conjunctivitis after every tuberculin inoculation for treatment.

Subcutaneous Tuberculin Test

As in the case of a local test, the subcutaneous test is also a specific reaction to hypersensitiveness on the part of the individual,—the difference being in the degree, as a constitutional reaction also takes place, due to the absorption of the tuberculin in this method of administration. As a direct result of the tuberculin inoculation, as given in this form of the test, we get a focal reaction at the point of the disease, which phenomenon reveals the place of infection and to a greater or lesser degree the activity of the process. Care must be taken to distinguish this reaction by becoming thoroughly acquainted with the condition previous to the injection. It is safe in the hands of the practitioner, provided the divisional method of administration is resorted to, as herein described, so as not to produce too violent a reaction with an active lesion.

Several examinations of the patient are necessary before the test, in order to recognize the focal reaction.

A description of a detailed technique for a subcutaneous inoculation would seem superfluous as every physician has had experience with the hypodermic syringe. Still, when we consider for a moment that an individual will have to submit to a large number of inoculations, anything that the physician can do to eliminate pain at the time of inoculation or prevent severity of a local reaction that may be brought about by a greater traumatic reaction, will be desirable. In this connection two important points are worthy of

Technic of the subcutaneous tuberculin test.

mention. First, have the arm where the inoculation is given in such a position that the needle easily penetrates the skin, and the physician is able to tell that the point of the needle is in the subcutaneous tissue. Second, the tuberculin should not enter intracutaneously, thereby avoiding an undue amount of traumatic reaction. Both these objects can be accomplished by rendering tense the skin through which the needle must penetrate. It will then feel as if the needle penetrates a membrane entering a vacant space beyond which is the subcutaneous tissue. The best way to render the skin tense is by grasping the arm from behind, drawing all the tissues backwards, as shown in the illustration. (Fig. 6.)

This will be found to be an improvement over the usual method of pinching up the skin when giving a hypodermic injection. Pressing the tissues together makes it impossible, at times, to tell whether the needle has penetrated into the muscular layer.

It is also advisable to bear in mind that the finest gauged needles can be used and that the points must at all times be sharp especially where there is a tendency to leakage from the puncture in the skin. Such an occurrence may sufficiently vary the amount of tuberculin absorbed to produce a sudden severe constitutional reaction during the treatment. The loss of tuberculin from such oozing may be very small in amount or, it may even amount to the entire dose given. It is therefore necessary to guard against such an occurrence by placing the cotton tipped applicator (or toothpick) dipped in iodine, over the point of puncture immediately upon withdrawing the needle. The same applicator that was used in painting the small area of skin with iodine, preparatory to inoculation may be used. It need not be dipped again in the iodine before this procedure, as a second application of iodine to the same spot may cause local irritation on a tender skin, especially if the iodine happens

FIG. 6.—THE SUBCUTANEOUS TUBERCULIN TEST.—The skin is rendered tense by drawing the tissues towards the back of the arm with the left hand, while plunging the needle with the right hand through the center of the area painted with iodine.

to be old. (Fig. 7.) The applicator is held there for a moment or two, using a little pressure, a drop of collodion being placed over the needle puncture after withdrawal of the applicator. Massage after a tuberculin inoculation should never be resorted to, as it is desirable to have the absorption of the tuberculin take place as slowly as possible from the point of inoculation.

In the event reinoculation is necessary, it should be made at a considerable distance from the former inoculation, as a local reaction may take place in the tissues that have been somewhat sensitized from a previous inoculation, where such a reaction would not have taken place otherwise. The result of this would be a false finding. It is better still to use each arm alternately for repeated inoculations.

SYMPTOMS OF THE TUBERCULIN REACTION

The principal elements in the general reaction elicited from a subcutaneous injection consists of the three principal elements: local reaction, the constitutional or febrile and the focal or lesion reaction.

Local reaction. The most frequent symptom of a general reaction is the reaction at the point of injection. This consists of a painful swelling at the site of the injection, with an infiltration of the subcutaneous tissue to various degrees around it. So frequent is the occurrence of a local reaction in a general reaction, that its non-occurrence usually throws doubt upon the interpretation of the rise in temperature as a general reaction. One must, however, be careful in the search for a local reaction, for it sometimes occurs in the subcutaneous tissue without producing superficial redness, and only careful feeling over the point of injection will reveal the small subcutaneous indurated mass. (Fig. 8.)

A hardened nodular induration at the point of inoculation constitutes the local reaction.

Constitutional reaction. With the constitutional manifestation of this reaction, we have a disturbance of the general health, by symptoms of varying degrees. The severe forms begin with a rigor, followed by sensation of heat or

The constitutional reaction resembles in its symptoms influenza, the symptoms disappearing in a surprisingly short time.

by a chill with an intense headache, accompanied by malaise, dizziness, nausea and even vomiting. This is soon followed by pains in the limbs, dragging or a sensation of pressure in the affected part, accompanied by loss of appetite, thirst, palpitation and sleeplessness. All these symptoms disappear with a fall in temperature, leaving a feeling of weakness lasting a day or two. All these symptoms last a surprisingly short time, considering their severity and nearly all symptoms disappear within forty-eight hours. The variability in the constitutional symptoms is great and depends entirely upon the individual constitution. Thus, we may have a very high rise in temperature, to 103 or 104, without the least subjective manifestation, or we may have a temperature rise of only one degree with the severest subjective symptoms. When carefully conducted, there should be no appearance of extreme constitutional symptoms and the temperature should never rise above two degrees. The usual appearance of a reaction takes place during the second twelve hours following the inoculation. However, it sometimes appears as early as four or five hours after inoculation and occasionally does not appear before thirty to thirty-six hours after inoculation.

The constitutional symptoms of the reaction usually appear during the second 12 hrs. after inoculation.

The focal reaction is the diagnostic feature of the test.

Focal reaction. The focal reaction is the distinguishing feature of the subcutaneous tuberculin test. It not only determines the presence of active tuberculosis and its extent, but very often helps to determine the location of the tubercular processes, which remained undiscovered. For instance, tenderness, which did not exist before will appear over a beginning affection of the spine during the tuberculin reaction; tenderness over the sternum with a feeling of pressure in the chest will reveal as a result of focal reaction, tubercular thoracic glands, on account of their swelling. A focal reaction is a transitory increase of the inflammatory process in the tubercular area and its manifestation will bring out the symptoms which go with an inflammation of the particular organ which it affects.

FIG. 7.—THE SUBCUTANEOUS TUBERCULIN TEST.—The needle is not withdrawn until the applicator with cotton on the end is placed over the injected area, ready for the pressure to be put over the puncture on withdrawal of the needle, to prevent loss of tuberculin through oozing.

FIG. 8.—THE SUBCUTANEOUS TUBERCULIN TEST.—The local reaction as it appears in the majority of instances and designated on the Treatment Charts as moderate.

Treatment of the constitutional symptoms.

Treatment of constitutional reaction. Regarding treatment of the reaction, only a few words are necessary. For the severe forms, rest in bed, with perhaps one or two doses of the coal tar products for severe headache, is all that is necessary. I warn particularly against the use of antipyretics, as we want the highest point of temperature revealed. In less severe forms, there is no necessity of keeping the patient in bed, avoiding manual labor or tiring exercise is sufficient.

PART II

TUBERCULIN IN TREATMENT

CHAPTER I

EQUIPMENT

Although it has been my aim in writing this book to simplify the treatment of tuberculosis to the greatest possible degree, there are certain details so essential to the success of the treatment, that one has to familiarize himself with them at once and give them his closest attention. I have endeavored to set these down under a separate chapter before going into the matter of the treatment of the various forms of tubercular affections in order to show at a glance all that is necessary to begin with.

I have come to the conclusion that it is not sufficient to merely make mention of these various items dispersed throughout a work of this kind, as in this way important details will very often be overlooked and so lead to much embarrassment and to complete abandonment of this important treatment. Again, the amount of detail will be seen to be far less burdensome if put down and explained at the outset, than if it has to grow upon the reader during the theoretical and practical discussions of the various phases in the treatment. In fact, after a careful perusal of this chapter, it will be noticed how simple after all, the armamentarium of the practical immunizator need be.

The simplest equipment possible is sufficient. The necessity for more elaborate equipment we will leave for experience to discover.

As regards the more elaborate paraphernalia described in other works—these were suggested with the specialist in mind and were prompted by a desire for completeness of their discussion. One may take advantage of these suggestions after the treatment of several patients when the whole subject will no longer be new and the mysteries surrounding it will have vanished. These suggestions represent the refinements that come with experience, rather than the

actual requirements of the condition. And since they only help to complicate the subject from the beginner's point of view—I thought it wiser not to touch upon the more complicated equipment in this work.

Proper Record Sheets or Cards

No one should attempt to use tuberculin or vaccine without keeping a careful record of the amount and date of each dose with the results following each dose; the weight of the patient and a record of various other data, such as laboratory findings, X-ray findings and other data during treatment of the patient. A chart in the form of a folder (thus having four pages) can have the history and diagnosis on the first page. The second page can be properly ruled for the record of the tuberculin administrations. This page should be ruled in eight parallel columns, the first for the date, the second for the number of the inoculation, the third for the number of the dilution used, the fourth for the quantity of tuberculin inoculated, represented by the amount of the particular dilution; two columns for reactions, one for the local and the other for the temperature; the seventh column for the weight record and the eighth for miscellaneous remarks. (See Fig. 9, page 45.) The sheet may be large enough to accommodate a double series like this on the one side of the folder, and will thus have room for 100 treatments, which is more than sufficient in most instances. Page three is divided into two parts, one-half for additional notes and the other half as a record for other medication. Page four can be used for the record of vaccines for mixed infections. Within the folder can be kept various laboratory reports, X-ray photographs and temperature charts. The whole sheet is made of heavy paper and measures 15½ inches in length and 8 inches in width and is so folded that the right hand sheet is one-half inch wider than the left, allowing the half inch to be visible for the name and diagnosis, and for filing purposes. During treatment it may be filed under

Proper records are essential.

the name of the patient and after the treatment, it may be compiled under the form of the disease.

It is difficult to conceive how any physician would fail to keep the proper records when treating a condition with tuberculin, for every dose is figured from the preceding doses under any form of tuberculin administration. Even were he able to remember all the quantities injected over a period of months, it is reasonable to suppose that no one would prefer burdening his memory, to the simple procedure of writing down a quantity; still, the following is an example: The patient, a little girl, eight years old, with a tubercular knee joint. The physician commenced treatment of this child with tuberculin after a single visit to my clinic at the New York Polyclinic Hospital. After five months' treatment, the physician died. The father of the child wrote to me asking whether I would continue the treatment of his little girl. My answer was in the affirmative and I requested that he bring a record of all the treatments the child had received up to that time. The following is a transcript of the letter that he brought to me, written by the former assistant and successor to the physician:

> Dear Mr. L.
>
> Here is a record for A., as per your request. Do not remember how many times we omitted the injection of the tuberculin, as we did not make a record of it—only the calls.
>
> Feb. 2
> Mar. 6-23-27
> Apr. 5-7-12-15-21-25
> May 2-6-10-13-16-20-24-27
> Jun. 3-8-13-19-23
>
> Hoping this will be satisfactory, I am,
>
> Yours very truly, Dr. X.

It is needless to state that the child had not improved in that time and the father expressed great disappointment over the fact, as he was led to believe that the child would

Name..... *Address*..... *Date*.....
Age..... *Nativity*..... *M. S. W. D.*..... *Occupation*..... *Sex*.....
HISTORY.....

DIAGNOSIS.....

FIG. 9—History page.

Date	No.	No. Sol.	Quant. c. c.	Reaction Local	Reaction Temp.	Wgt.	REMARKS	Date	No.	No. Sol.	Quant. c. c.	Reaction Local	Reaction Temp.	Wgt.	REMARKS
	1								51						
	2								52						
	3								53						
	4								54						
	5								55						
	6								56						
	7								57						
	8								58						
	9								59						
	10								60						

FIG. 10—Tuberculin record page of the record folder used by the author.

be cured in from six to eight months. It might also be mentioned here that no temperature record of the child had ever been kept during the treatment; and the father expressed surprise when he was instructed to keep such a record and told that we could not treat the child without the temperature being taken after each inoculation.

Syringe

A Record tuberculin syringe or all-glass tuberculin syringe is best.

The use of the proper syringe will obviate the necessity for a study of the metric system in case one is not familiar in it. I have found in my teaching that quantities measured in any other way than minims and drams were meaningless. The everlasting question when a quantity of tuberculin is mentioned in the lecture is: "How many minims is that?" But the minim measurement is out of the question in the administration of tuberculin, as we cannot give parts of minims and one minim is equivalent to approximately 0.06 c.c., which is three times the amount of increase advised at the beginning of treatment. The further diluting of each dilution to make a minim equivalent to 0.02 c.c. will complicate the subject a great deal; whereas, with little trouble, one can obtain the proper syringe. The Record tuberculin syringe is the best for general use. It holds one cubic centimeter, which is divided into ten large divisions. Each large division, which holds a tenth of a cubic centimeter, is subdivided into fifths, each small division therefore holds one-fiftieth or 0.02 c.c. Whether one understands the metric system or not, one merely measures the dose by drawing into the syringe the amount desired, the reading of that quantity is on the barrel of the syringe. All glass syringes that are made in this country are even more finely subdivided, each division holding 0.01 c.c. Difficulties are sometimes experienced with these syringes, owing to the slipping of the piston in the barrel. This has to be guarded against by pressure with one finger on the piston where it enters the barrel. Some of these syringes are now provided with a metal spring for that purpose. (See Fig. 1, page 14.)

Needles

The needles should be of very fine caliber in order to avoid traumatic reaction.

Since tuberculin is not very viscid, the finest gauged needles should be used. This is important,—on account of the large number of inoculations necessary during treatment, making it desirable to avoid as much discomfort as possible to the patient and to prevent traumatic reactions. A platinum-irridium needle may be used, as its advantage over the plain needle is that it can be sterilized in the flame. But where an all glass syringe is used, a cracking off of the screw end or slip end of the syringe very often occurs. The plain 25-gauge needles one inch long, are inexpensive, can be readily obtained and serve the purpose as well as any other needles made. The syringe and needles are sterilized in alcohol and rinsed with the diluting fluid before treatment.

Office Scales

Office scales are essential.

All office balance scales will do for weighing the patients. A physician should not depend upon his patients' weighing outside and bringing in their weight for record. It is seldom that a patient will take the trouble to remember the difference in clothes between each weighing; whereas, in the office one can weigh the patient right after the inoculation. One can always follow a given routine in the office for weighing patients in order to have any extraneous influences eliminated.

Containers for Dilutions. (Figs. 3 and 4.)

Any bottles holding a little over a cubic centimeter are suitable. If the bottles are so large as to prevent the needle from reaching the bottom, the mouth of the bottle must be large enough to admit the circumference of the syringe. These bottles may be sterilized by allowing them to remain over night, filled with 95 per cent. alcohol. This alcohol must be rinsed out with diluting fluid before making dilutions. Small squares of adhesive plaster may be

used in labeling the bottles. A cool, dark place for the storage of the tuberculin and vaccines completes the equipment.

Instructions to Patients

Aside from instructions as to taking of temperature, it is best to limit the first consultations to the diagnosis of the disease.

Aside from the usual instructions as to hygiene, diet and fresh air,—details into which we need not go here,—the patient should be instructed in the regular taking of temperature four times daily: at eight, at twelve, at four and at eight o'clock, for at least three or four days,—and should be taught to keep a careful record of it. No other instructions that refer to tuberculin treatment need be given at the first consultation. The patient's mind is diverted entirely to the realization of his condition; and any other discourse or instruction will lose its force if given at the same time with the diagnosis. However, the carrying out of the instructions for taking temperature will prevent in a measure the brooding and worry, and will add to his confidence in the physician.

At the subsequent visit, all instructions as to hygiene, diet, etc., should be given.

At the second visit, the patient should be told the meaning of immuno-therapy; he should be told that tuberculin administered twice weekly will stimulate his own protective processes, helping him in that way to overcome his disease. The prejudices existing against tuberculin must be mentioned to the patient, so that if they have not reached his ears before, his confidence in tuberculin during treatment should not be lessened by what he may hear from outside sources. It must also be explained that these prejudices were brought about by the faulty administration of tuberculin, and that with a more careful technique, tuberculin is devoid of danger. It must be especially emphasized to the patient that the treatment must be brought to a conclusion when once it is begun, as an interruption of the treatment before maximum tolerance is reached will often lead to a rapid retrogression of the condition. This retrogression following upon a too early discontinuation of treatment has often been laid to the tuberculin itself. Indirectly, it may

be true; for, just as the sudden discontinuation of stimulants in heart disease may sometimes cause a sudden collapse of the heart muscle; so also in tuberculosis, when the healing process depends upon outside stimulation, which when prematurely discontinued will cause sudden retrogression. We must therefore continue the treatment with tuberculin to the point of maximum tolerance and then for a period of time, determine at regular intervals whether the maximum tolerance is being maintained. (See Tri-Monthly Tests, page 147.)

The patient must also be made to understand that the proper administration of tuberculin depends a great deal upon his own assistance; that he is a "partner" in the treatment, and therefore must take his temperature regularly every two hours, on the day of the inoculation and the day following it. He must note as far as possible any focal manifestation and mention it to the physician when he next presents himself for treatment. The focal manifestations must be explained as an increase in the various signs and subjective symptoms, and the patient must note how long this increase persists after the inoculation, so that we may be able to differentiate between an actual focal reaction and a retrogression in the disease, due perhaps to insufficient tuberculin.

The patient must be a willing partner in the treatment to insure its success.

It is by far better to instruct the patient to take rectal temperature, if convenient. However, if that be impracticable, and the mouth temperature must be depended upon, the patient should be instructed to make certain that the mercury column in the thermometer is shaken down below 95° before taking the temperature and that he keep it under his tongue for at least five minutes by the clock, even if the thermometer be a "one-minute" thermometer. The physician need not expect to meet with any difficulties in the carrying out of his instructions with regards to temperature. If he insist that the treatment will depend upon the proper taking of temperature and will absolutely refuse the treatment if the patient pleads ignorance in the matter, it is

The most illiterate patient can be made to keep an accurate temperature record.

surprising what ability will be displayed along this line by the most ignorant patients. It was said, when I first established a clinic, that if my treatment depended upon the taking of temperatures by the patients, the whole project would prove a failure, for the class of patients who apply for treatment at the New York Polyclinic Hospital consists mainly of the ignorant foreign element. In spite of that assertion, the clinic has grown larger in size and every patient who gets the treatment brings on paper his temperature succeeding his last treatment. It is a matter of comment to see what surprisingly neat temperature records these patients bring. The difficulty, if met with, consists of the inability on the part of the patient to get the focus upon the mercury column in the usual magnifying thermometer. The plain thermometer without the magnifying glass can be obtained through any druggist and will remove the only difficulty in the way of the patients reading the temperatures.

In ambulatory cases, I have avoided complicating the treatment from the standpoint of the patient by refraining from the distribution of printed slips, requiring the answer to many questions concerning pulse, respiration, headache, pain in the limbs, pain in the joints, malaise, sleeplessness, fatigue, restlessness, nervousness, indigestion, nausea, vomiting, chilliness, rash, enlarged glands, and a host of other questions which are printed on slips and distributed among patients in many clinics. I am quite certain that seventy-five per cent. of the answers are influenced by the concentration upon the symptoms. It is quite sufficient to ask the patient at the time of his visits whether he has coughed more or less, whether he brought up an increased amount of sputum or whether there was a noticeable decrease; whether the amount of discharge from a sinus is markedly increased as shown by the amount of increase of dressings required and whether this discharge is thinning or becoming thicker; and in a case of glands, whether they have become more swollen or less swollen, or more painful or less painful, and so on through the different varieties of tuberculosis.

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Chapter II

TUBERCULIN TREATMENT

The methods of treatment with tuberculin resolve themselves into three distinct classes: the reactive method, the non-reactive method and the combination of the two. The reactive method is the one that Koch originally used, and has but few remaining adherents at the present day. It consists of giving a dose sufficient to cause reaction, and continuing with the same dose every third or fourth day;—each time producing the same reaction. The sudden collapse of tuberculin therapy that marked the first tuberculin era was brought about by this treatment, as disastrous results overtook the largest majority of patients treated by this method. The fear that overtakes most physicians at the suggestion of tuberculin therapy has been instilled by this method of treatment; a fear which the great majority of physicians try to mask by condemnation. Why base this condemnation on ignorance and hearsay, instead of dispelling it by investigation and fair trial? We must remember that this method of treatment was born of a desire to find a remedy for so important a disease as tuberculosis before the hypersusceptibility existing in this disease was known and the desire for an immunizer was so great that its use was attempted far too generally before its true nature was understood. The disappointment that soon followed was consequently so intense that condemnation of tuberculin took the place of further study and investigation.

The three methods of tuberculin administration are the reactive, the minute dose, and the one that combines the two.

Fortunately, there were a few investigators who were quick to recognize the indication of its virtues and who continued the use of tuberculin and evolved the second method of treatment; the non-reactive method. It was quite a natural outcome to revert to minute doses after the larger doses had proved unsuccessful. The minute dose was used in the same way, as the larger dose was used, merely inocu-

The minute dose method led to the stimulation of the hypersusceptibility and thereby never attained complete tolerance.

lating at three to seven-day intervals, the same minute dose or very slightly increasing it. There are still at the present day those who report fairly good results with this method, but further investigation has proved that the hypersusceptibility can only be reduced by increasing doses, that the same dose has no further effect upon the hypersusceptibility after one or two inoculations. In fact, experience has shown that when the small dose is kept up for any length of time, the hypersusceptibility increases; a distinctly harmful effect in such favorable cases where tuberculosis is quiescent and the hypersusceptibility is not very marked. However, this harm is very often overlooked and because of its insidious appearance, is laid to the progress of the disease and not to the method used in the tuberculin administration.

A method now in use, while better than the other two, still remains limited to well chosen cases.

The third method and most generally used at the present day is the method which consists of small doses increased according to the amount of hypersusceptibility in each individual case. It is well known that to obtain toxic immunity, we must begin with the dose less than we require to produce toxicity, this dose being increased in proportion to the acquired tolerance of the individual. With that in view, methods of dosage have been devised, which depend upon a mathematical increase of dosage entirely too rapid or too large for the majority of patients—the increase in tolerance not keeping pace with the increase in tuberculin. Severe reactions are frequently encountered—thus making the choice of patients for tuberculin treatment absolutely necessary. Only long experience and expert judgment can bring about a fair amount of accuracy in the choice of the patient,—a fact that stands out most prominently against the wider adoption of tuberculin therapy.

A closer analysis of the principles involved in the physiological action of tuberculin with a view to simplifying tuberculin therapy, brought out the following facts:

FIRST: The dose of tuberculin has no effect, if it is less than the maximum amount that can be tolerated without any reaction on the part of the individual.

SECOND: It requires more tuberculin to reach the amount of maximum tolerance at each succeeding dose.

The principles involved in the physiological action of tuberculin.

THIRD: The subsequent doses, although larger than the first in amount, have no effect if the first dose was less than the maximum amount that could be tolerated by the individual and if the amount of increase is not enough to bring the total to the maximum amount of tolerance.

FOURTH: That any constitutional reaction, however mild, increases the amount of hypersusceptibility and the maximum amount of tolerance thereby decreases, thus requiring a diminution of the dose following such a reaction.

FIFTH: The only index to the measure of tolerance in every individual is a constitutional reaction, hence a constitutional reaction is desirable in every case.

SIXTH: Since a constitutional reaction lowers the point of tolerance, we must be sure to make such a reaction as mild as possible in order not to lower the tolerance to too great a degree.

An early experience in otherwise hopeless cases afforded me the best opportunity for a careful elaboration of these principles for practical purposes. I found that all these principles could be incorporated in a system of dosage, which begins with a certain amount of tuberculin, increasing the dose subsequently by a definite amount for a certain number of treatments and then increasing the increase at definite intervals until a reaction is reached. The reaction thus produced is mild, because it is produced by the smallest amount of tuberculin required to produce such a reaction in the individual, taking account of the increased tolerance produced by previous injections. By increasing the intervals, after such reaction, and decreasing the dose by a small amount, to offset the decreased tolerance produced by the reaction, we know that we are using a quantity of tuberculin as nearly exact for that particular indivdual as can be approximated to produce the ideal therapeutic effect. For the next

The harm from the reactions obtained by this method is insignificant.

few treatments, therefore, the increase need be but slight in order to keep up this full therapeutic effect, and so this increase is begun at this point as at the beginning of treatment, subsequently increasing this increase again, to make sure that we do not fall behind in producing the maximum effect. A second reaction may thus be reached and even a third, during a course of tuberculin treatment, and since these reactions cannot be but mild, the continued maximum effect produced by thus constantly keeping at the level of maximum tolerance, far outweighs the possible ill effect produced by such mild reactions.

Explanation of Dosage Table I, (Page 57.)

Explanation of doses.

If the treatment requires that we begin with the fifth dilution and having 0.10 c.c. as the first dose, the second dose would be 0.12 c.c., the third dose 0.14 c.c., thus increasing twice by 0.02 c.c. At the third dose, however, the increase should be increased by 0.02 c.c., the total increase therefore would be 0.04 c.c., making the third dose 0.18 c.c. We increase a second time by 0.04 c.c. making the fourth dose 0.22 c.c., again increase the increase by 0.02 c.c. at the fifth dose, making the total increase 0.06 c.c. and the fifth dose 0.28 c.c. At the sixth injection, the increase is the same as at the fifth, making the quantity of the sixth injection 0.34 c.c., but at the seventh injection we add 0.02 c.c. again to the increase, making the total increase now 0.08 c.c. and the quantity for the seventh injection will thus be 0.42 c.c., repeating the same increase for the eighth injection, we have as our eighth dose 0.50 c.c. This goes on, increasing the increase at every second treatment by 0.02 c.c, until a full cubic centimeter or nearly a full cubic centimeter is reached, when the treatment should begin with a 0.10 c.c. of the fourth dilution. Beginning again with an increase of 0.02 c.c. and continuing the dosage with the fourth dilution as with the fifth dilution, so also with the third dilution and with the second, until the first dilution is reached.

By the time the first dilution is reached, the tolerance of the patient is usually so high that the increase in the dosage may be increased at every injection, instead of at every other injection. Thus beginning with 0.10 c.c. of the first dilution, the second treatment should be 0.12 c.c., which is an increase of 0.02 c.c. The third injection should be 0.16 c.c., being increased by 0.04 c.c., the fourth treatment is 0.22 c.c., which is an increase by 0.06 c.c. The fifth treatment is 0.30 c.c., making the increase 0.08 c.c., and so on until a full cubic centimeter of number one is reached, making the conclusion of the treatment with OT. A careful perusal of the Table of Dosage, page 57, will illustrate its simplicity. Should a constitutional reaction occur after any one of these injections, an interval of a full week is indicated before resuming treatment, commencing then with the third last dose as illustrated in Table of Dosage II, page 59, The treatment is then continued as before, but the amount of increase should be as at the commencement of treatment, no matter what the quantity of increase was before the reaction. Thus, if a reaction occurs after 0.18 c.c. of the fourth dilution, the next dose should be 0.12 c.c. of same dilution, followed by an increase of 0.02 c.c. for two consecutive treatments, then by 0.04 c.c. for two consecutive treatments and so on as before.

Table of Dosage II also illustrates the effect of a local reaction on the subsequent dosage—that is, a local reaction has no effect on the quantity to be inoculated, but does require the lengthening of the interval to a week.

Intervals

Tuberculin is administered twice weekly.

Tuberculin injections should be given twice a week, arranging for the new increase just before the longer of the two intervals. In administering two injections a week, we have an interval of two days and another of three days, and since the increase of the increase is made at every second injection, it could be so timed as to fall before the three day interval.

A local reaction should lengthen the interval before the next treatment to a full week.

A *local reaction* persisting at the time when the next treatment is due should indicate a postponement of the treatment, lengthening the interval to a week; a local reaction still persisting beyond a week has no further significance. Neither does a local reaction, when it is not accompanied by a constitutional reaction, indicate a lessening of the dose.

A focal reaction should not influence the course of the treatment except in isolated instances.

As I have stated in another chapter, a *focal reaction* is merely a manifestation of the therapeutic and physiological action of the tuberculin and need not at any time indicate either reduction in dose or lengthening of interval. However, in lung cases where there is a tendency for hemorrhage and the focal reaction brings forth blood streaked sputum, it is well to increase the interval to one week and in cases where the danger of hemorrhage is more pronounced, it is best not to increase the increase until this tendency disappears. An increase in dose by 0.02 c.c. or 0.04 c.c. can be maintained even during the presence of blood streaked sputum.

A temperature reaction indicates a decrease in the next dose, an increase in the interval before the next dose to a full week, and the return to the original amounts of increases.

The *constitutional reaction* indicates the increase of the interval to one week, and also a reduction in the amount of tuberculin—making the treatment following the constitutional reaction equal to the third last dose and the return to the smallest increases as at the beginning of treatment. Should a constitutional reaction occur after the first treatment, the interval before the next treatment should be a week and, as was stated elsewhere, the treatment is resumed with one dilution higher. For example: If a reaction occurs after beginning treatment with a 0.10 c.c. of No. 4, the following injection should be 0.10 c.c. of No. 5, with treatment from there on as if dilution No. 5 were the first used. When 0.10 c.c of No. 5 at the first injection produce a constitutional reaction, a sixth dilution must be made and used in the same dosage as dilution No. 5 would have been used.

Table of Dosage I

SHOWING SCHEME OF DOSAGE WITHOUT REACTION

Date.		No. of Treat.	Dil. No.	Quant per c. c.	Reaction Local	Reaction Temp.	
Jan.	1	1	V*	0.10	0	0	
	5	2		0.12			+0.02
	8	3		0.14			+0.02
	12	4		0.18			+0.04
	15	5		0.22			+0.04
	19	6		0.28			+0.06
	22	7		0.34			+0.06
	26	8		0.42			+0.08
	29	9		0.50			+0.08
Feb.	2	10		0.60			+0.10
	5	11		0.70			+0.10
	9	12		0.82			+0.12
	12	13	IV	0.10			
	16	14		0.12			+0.02
	19	15		0.14			+0.02
	23	16		0.18			+0.04
	26	17		0.22			+0.04
Mar.	1	18		0.28			+0.06
	5	19		0.34			+0.06
	8	20		0.42			+0.08
	11	21		0.50			+0.08
	15	22		0.60			+0.10
	18	23		0.70			+0.10
	22	24		0.82			+0.12
	25	25	III	0.10			
	29	26		0.12			+0.02
Apr.	1	27		0.14			+0.02
	5	28		0.18			+0.04
	8	29		0.22			+0.04
	12	30		0.28			+0.06
	15	31		0.34			+0.06
	19	32		0.42			+0.08
	22	33		0.50			+0.08

	26	34	0.60	+0.10
	29	35	0.70	+0.10
May	3	36	0.82	+0.12
	6	37	II 0.10	
	10	38	0.12	+0.02
	13	39	0.14	+0.02
	17	40	0.18	+0.04
	20	41	0.22	+0.04
	24	42	0.28	+0.06
	27	43	0.34	+0.06
	31	44	0.42	+0.08
June	3	45	0.50	+0.08
	7	46	0.60	+0.10
	10	47	0.70	+0.10
	14	48	0.82	+0.12
	17	49	I 0.10	
	21	50	0.12	+0.02
	24	51	0.14	+0.04
	28	52	0.22	+0.06
July	1	53	0.30	+0.08
	5	54	0.40	+0.10
	8	55	0.52	+0.12
	12	56	0.66	+0.14
	15	57	0.82	+0.16
	19	58	OT 0.10	+0.18
	26	59	0.20†	

* If reaction occurs after this dose, begin treatment with the sixth dilution. The dosage of the sixth dilution being the same as the fifth.

† Double last dose as a test for any possible remaining hypersusceptibility. If there is a reaction to this dose, repeat the entire course of treatment with No. 1.

Table II

SHOWING THE EFFECT ON DOSAGE AND INTERVALS OF A LOCAL REACTION AND A CONSTITUTIONAL REACTION

Date.		No. of Treat.	Dil. No.	Quant. per c. c.	Reaction Local	Reaction Temp.	
Jan.	1	1	V	0.10	0	0	
	5	2		0.12			+0.02
	8	3		0.14			+0.02
	12	4		0.18			+0.04
	15	5		0.22			+0.04
	19*	6		0.28	+++	0	+0.06
	26*	7		0.34	++		+0.06
Feb.	2*	8		0.42	+		+0.08
	9	9		0.50	0		+0.08
	12	10		0.60			+0.10
	16	11		0.70			+0.10
	19*	12		0.82	+++	101°	+0.12
	26	13		0.60	0	0	3d last dose
Mar.	1	14		0.62			+0.02
	5	15		0.64			+0.02
	8	16		0.68			+0.04
	11	17		0.72			+0.04
	15	18		0.78			+0.06
	18	19		0.84			+0.06
	22	20		0.10			
	25	21		0.12			+0.02
	29	22		0.14			+0.02
Apr.	1	23		0.18			+0.04
		etc.		etc.			etc.

After each of the sixth, seventh, and eighth dose there was a local reaction with a temperature rise to 101°, therefore there is an interval number of crosses (+) merely designates the severity of the local reaction: thus one cross indicates a mild, two crosses a moderately severe, and three crosses a severe local reaction.

After the twelfth dose there was both a local and a constitutional reaction with a temperature rise to 101, therefore there is an interval of one week after the twelfth dose, and the quantity administered as a

* Interval of one week.

thirteenth dose reduced to the same as was given at the tenth inoculation. The fourteenth dose is only 0.02 c.c. larger than the dose given after the constitutional reaction or dose thirteen, for the increase after a constitutional reaction should be reduced to the same quantity as at the beginning of treatment.

Table III

BACILLARY EMULSION AFTER OT

Date.	No. of Treat.	Dil. No.	Quant per c. c.	Reaction Local	Reaction Temp.
Aug. 5	60	BE I	0.10	0	0
12	61		0.20		
19	62		0.30		
26	63		0.40		
Sept. 2	64		0.50		
9	65		0.60		
16	66		0.70		
23	67		0.80		
30	68		0.90		
Oct. 7	69	BE Pure	0.10		
14	70		0.20		

In cases where there is complete clinical cure and where the BE is given to make sure that we obtain a bacillary immunity as well as toxic immunity, it may be given as rapidly as indicated in this chart.

Table IV

BACILLARY EMULSION AFTER OT. SLOW METHOD

Date.	No. of Treat.	Dil. No.	Quant. per c. c.	Reaction Local	Reaction Temp.
Aug. 5	60	BE I	0.05	0	0
12	61		0.10		
19	62		0.15		
26	63		0.20		
Sept. 2	64		0.25		
9	65		0.30		
16	66		0.35		
23	67		0.40		
30	68		0.45		

Oct.	7	69	0.50	0	0
	14	70	0.55		
	21	71	0.60		
	28	72	0.65		
Nov.	4	73	0.70		
	11	74	0.75		
	18	75	0.80		
	25	76	0.85		
Dec.	22	77	0.90		
	9	78	BE Pure 0.10		
	19	79	0.12		
	29	80	0.14		
Jan.	7	81	0.16		
	17	82	0.18		
	27	83	0.20		
Feb.	6	84	0.22		
	16	85	0.24		
	26	86	0.26		
Mar.	5	87	0.28		
	15	88	0.30		

In cases where complete clinical healing has not taken place by the time OT is concluded it is best to administer BE by this slow method in order to keep the patient under its influence during treatment for the local condition. Open bone and joint cases very frequently take longer to completely heal the local condition than it takes to complete a course of tuberculin. Also in pulmonary cases with a cavitation, the cicatrization of the cavities might take a great deal longer than it takes to gain complete tolerance. In such conditions the administration of tuberculin should not be entirely discontinued until clinical healing has occurred.

Chart I is a schematic representation of the relation of tuberculin to a patient's tolerance. *A* represents the minimum tolerance, a state where the patient has lost the immune response and is absolutely hopeless.

C represents the level of maximum tolerance,—a state where the toxic immunity is complete and the hypersusceptibility has disappeared.

B represents the level of tolerance of a given tuberculous individual at the beginning of tuberculin treatment.

Curve X-Y represents a maximum rise of tolerance without reaction and in response to an ideal method of tuberculin inoculation, were we in possession of an accurate method of measuring tuberculin to individual hypersusceptibility.

(a) is a curve showing the influence of a tuberculin inoculation on the patient's tolerance—when the first dose is too small to cause a reaction and the same dose is always repeated;—after producing no result for a while, it would soon increase the patient's hypersusceptibility and even lead to a more rapid progress of the disease.

(b) is a curve showing the influence of a course of tuberculin inoculations on the patient's tolerance when the first dose is less than the patient can tolerate without a reaction—the dose being subsequently increased at every inoculation by the same amount—the increase not being sufficient to make up the difference between the preceding dose and the amount that would bring it to maximum tolerance. The curve would rise for a while, but would soon lose in effectiveness, until the tuberculin would fail to produce any results whatever.

(c) is a curve showing the influence of a course of tuberculin inoculations on a patient's tolerance where the first dose is as it should be—less than the patient can tolerate without reaction—and where the dose is increased and the amount of increase also increased. It thus makes up for the amount of tolerance gained by each previous inoculation and gains upon the patient's increasing maximum point of tolerance. Owing to our inability to judge when we are near the maximum point of tolerance, we may even exceed it on several occasions producing a reaction. This for the moment lowers the patient's tolerance. But, this lost ground can easily be made up, if with a proper technique we avoid too great a reaction and therefore too great a set-back. Such a set-back is advantageous, as it serves as a guide to the most

CHART I

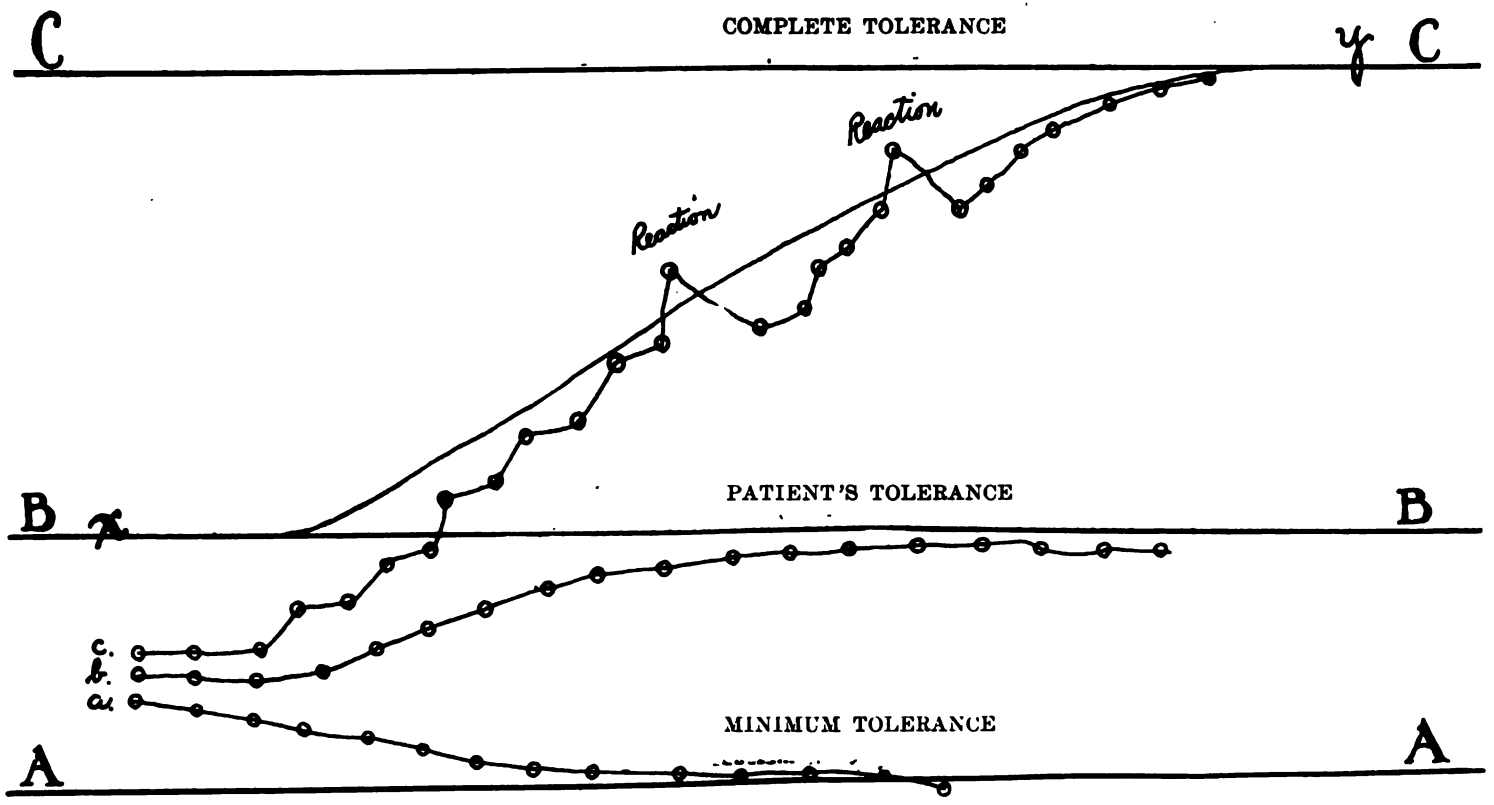

Diagram showing the effect upon the tolerance and hypersusceptibility of the
(a) the non-increased;
(b) the uniformly increased;
(c) the progressively increased method of dosage.

CHART II

COMPLETE TOLERANCE. DISAPPEARANCE OF SUSCEPTIBILITY

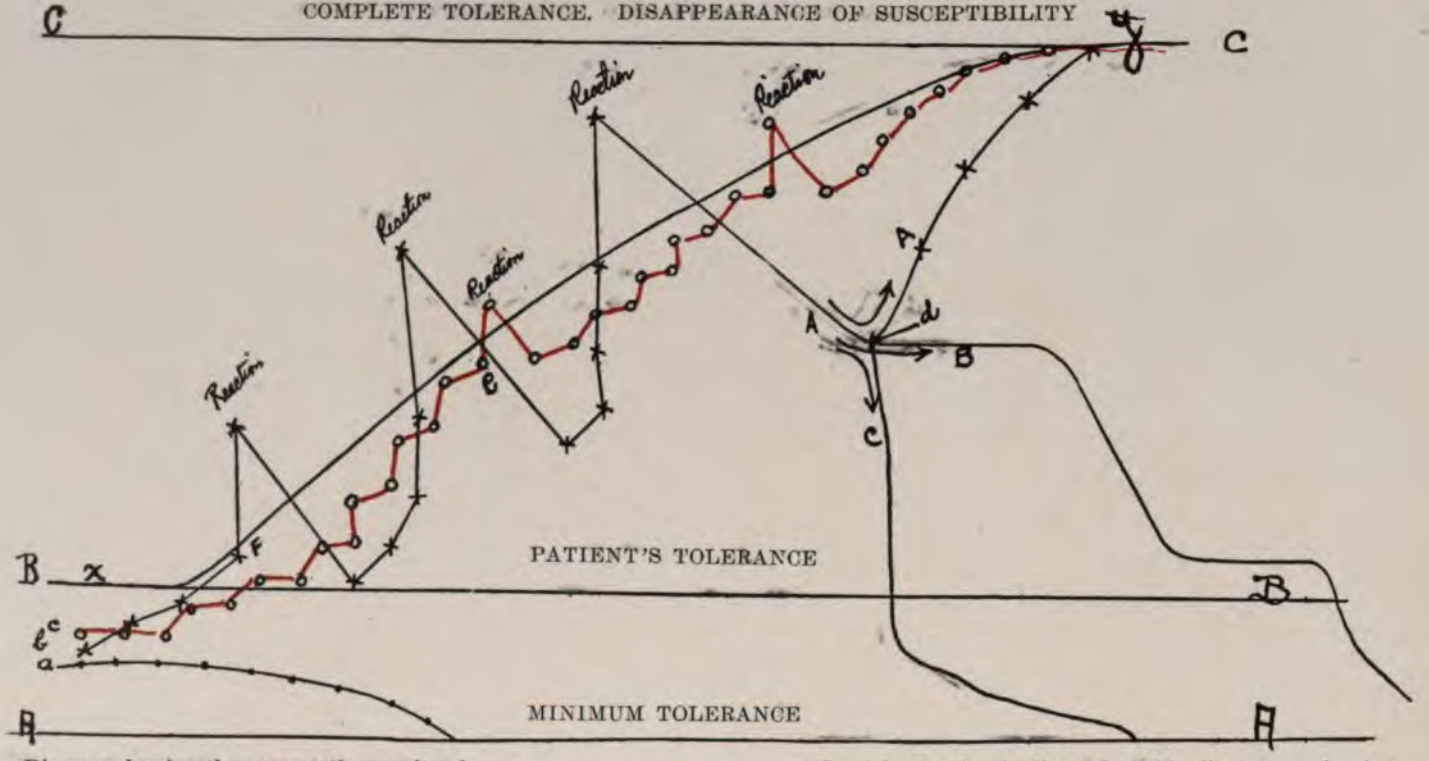

Diagram showing the comparative results of
(a) the minute dose method;
(b) the present method in use;
(c) the author's method of tuberculin treatment.

Special attention is directed to this diagram as showing why the *choice* of the patient was heretofore necessary for tuberculin treatment, whereas with the author's method tuberculin may be almost universally applied.

effective method of tuberculin therapy, the method which keeps the patient at maximum tolerance.

Chart II is a schematic representation of the three methods of tuberculin administration and their effect upon the patient and their comparative success in removing hypersusceptibility. As in Chart I, A and C represent the minimum and maximum levels of tolerance and B the level of tolerance of a given individual at the beginning of tuberculin administration. X-Y represents the ideal tolerance curve as in Chart 1. (a) represents a curve showing the effect of the minute dose method of administration. This method has been almost abandoned, for it leads to no effect at all or to an increased hypersusceptibility (lowered tolerance). (b) represents the effect of the present-day method of tuberculin administration, in which every dose is increased considerably, as by the logarithmic method. In this method the maximum point of tolerance is soon reached, as at (f) and the immunizator not being aware of the fact, proceeds with the increase which is equivalent to approximately one-half of the preceding dose. This will cause quite a severe reaction as indicated by the height of the curve. The drop in the curve represents the increased susceptibility together with the lowered tolerance, following such a reaction. The reduction in the dose will soon raise the tolerance of the individual with the ultimate production of another reaction. Several reactions may be produced during the treatment until one of the reactions will be followed by such heightened hypersusceptibility, as to cause alarm, as represented at (d). At this point, three different things may happen depending upon the condition of the individual and the attitude of the physician administering the tuberculin. The patient may possess good resistance, recuperate from the depression and have the tuberculin administrations resumed with greater care, and as represented by arrow A-A, the patient will be brought to maximum tolerance and a cure accomplished.

Again, at this point, (d) the physician will lose confidence in tuberculin, abandon its use, and as represented at A-B, the patient's susceptibility will remain at the level for a while, and then will slowly descend with the progress of the disease. As a third possibility, the last reaction may be so severe that the drop of the curve may rapidly continue as shown by A-C, a rapid progress of the disease will ensue and the patient's tolerance will be lowered to the minimum point. This is the method in vogue at the present time and one can see at a glance how, in the light of this method that it is necessary for the physician to be able to choose his patients so that they fall in the category of the first of the three possibilities. And since the choice of the patient requires a great deal of experience and special training, tuberculin therapy had to pass beyond the province of the general practitioner.

Curve (c) represents schematically the method of tuberculin inoculations the author has succeeded in working out. As in the other methods, it begins with a dose too small to cause a reaction and less than the patient's tolerance at the moment would justify. Increasing the dose by a small amount would keep it just as far from the patient's tolerance, but this increase is increased at every other inoculation, gaining thereby upon the patient's maximum tolerance until at point (e) it approaches the maximum tolerance. Owing to our inability to judge that maximum tolerance is reached, the next inoculation is increased and a reaction is produced. But this reaction is necessarily a mild one, as this method of increase allows of the production of such a reaction as would be brought about by the smallest amount of tuberculin possible to produce a reaction at that particular point of the patient's tolerance. There is a loss of tolerance following such a reaction, no matter how mild; but such loss is in proportion to the severity of the reaction, which being mild, produces a loss of tolerance equally mild. From this point on, the increases are resumed as at the beginning of treatment and since these increases are gradually increased

again, another reaction may be produced and perhaps several more during a course of treatment, but in each case it will merely serve as an index to the state of maximum tolerance of the individual. At no time are any of these reactions dangerous, permitting every case to acquire complete tolerance which is the goal of tuberculin therapy. It can thus be safely handled by the general practitioner.

Advisability of Acquiring Tuberculin Technique by First Treating Cases Where Severe Reactions will not be Dangerous.

The simplest technique is susceptible of errors,

No matter how simple a technique may be, it still requires some practical experience in order to divest it of the uncertainties with which it seems to be surrounded. Especially is this true of a technique which is dependent upon the constitutional effect of the therapy in question. This applies particularly to tuberculin, an agent which has acquired such a varied reputation that one cannot avoid a certain amount of fear and trembling when first attempting its use. The majority of general practitioners who awaken to the heralded virtues of tuberculin and who are led to begin its application among their patients, find themselves hampered by two important drawbacks to its effective use:

especially when one starts out without a conception of the nature of a tuberculin reaction.

One is the fact that they start out without any knowledge of the mechanism of the tuberculin reaction, nor of the literature which is written upon the use of tuberculin. They do not often delve into the enormous literature on the subject in order to get a fair perspective of the physiological mechanism involved, when the first case presents itself for treatment. They will commence the use of tuberculin inspired by a single report in the Medical Journal where one or two favorable cases may happen to be reported. Under such conditions, it is no wonder that the attempt results in a hasty discontinuation of the use of tuberculin. A poorly measured quantity, a mistake in the number of the dilution, a failure even to wash a surplus of pure tuberculin from the syringe

before taking a quantity of a weak dilution for inoculation, will cause a severe constitutional reaction with a proportional amount of disaster to the patient. Result: the tuberculin is discarded and a ready recruit is added to the ranks of the enemies of tuberculin. The prejudice against tuberculin will now step in to prevent a calm analysis of the effect produced in order to discover where the fault exists, which really is with the technique and not with the tuberculin.

It has been the tendency to use tuberculin as a last resort and then to decry its value in general.

The second factor that stands in the way of sufficient experience and fair trial for tuberculin therapy is the choice of the patient when a physician first decides to use tuberculin. Usually he will try every conceivable remedy and only when the patient is hopeless and almost at death's door, will he in desperation think of tuberculin and attempt its use. That the result must be negative is inevitable. And again we have the prejudice against tuberculin to help the physician attribute the loss of his patient to the tuberculin instead of to his failure to resort to it in time and to the hopelessness of the condition when first he attempted its use. One can readily see that such experiences with tuberculin do not only create adverse judgment in the mind of the physician who has had these unfavorable experiences, but will strengthen the prejudice among the greater or lesser circle in the community which is under his influence. It is the aim of this work to lay before the medical profession in as simple terms as possible the details of tuberculin therapy; but however simplified and simply expressed they may be, details they still are, and as such require attention. Yet it would be demanding the impossible to expect the beginner with a new technique to be perfect in every detail. But since in tuberculin therapy the oversight of such details may cause unpleasant symptoms and dangerous effects in the patients, and since such accidents cannot be avoided, it is advisable to choose tubercular conditions where such mistakes will do the least damage.

Such tubercular conditions are found among the cervical adenitis and lupus cases. The fact that the process is lim-

ited to the glandular system in the former, shows the great amount of resistance the patient possesses to tuberculosis. The patient is usually in robust health with no other discomfort except the enlarged glands. The severest constitutional reaction possible can consist of bodily discomfort lasting a day or two. Then recovery goes on even more rapidly at times after such an experiment; and if with a little care the exact cause of such a reaction is determined, overlooked details will receive due attention in the future. In this way each factor in the proper technique will become impressed upon the mind so that by the time the physician concludes the treatment of one single case, he shall have acquired almost a complete mastery over this technique.

Tubercular cervical adenitis and lupus are suitable conditions for first trial with tuberculin therapy.

Chapter III

TUBERCULOSIS OF THE GLANDS

Our present knowledge of the process of infection by the tubercle bacillus leads us to the conclusion that the tuberculosis of glands represents the primary form of tubercular infections. The most recent investigations regarding the entrance of the tubercle bacillus into the organism, and its future rôle as forming the various processes of tubercular infections, leads to the plausible conclusion that tuberculosis, like syphilis, has three stages. The infection of glands represents the first stage, and therefore comes mainly in early childhood; the infection of bones and joints represents the second stage and the infection of the lungs represents the third stage of the disease. It is not the point in question here whether the tubercle bacillus enters the peri-bronchial or mediastinal glands by way of the bronchioles; or, whether the mesenteric glands are infected by way of the bowel walls; or, whether the glands of the neck are infected through the tonsils; or, whether the bacillus gains entrance through inhalation or infected food. What is of interest to us from a practical point of view, is that infants rarely die of tuberculosis of the lungs as a primary infection; that as a general rule, the infections of bones and joints occur in children older than those affected with glands and younger than those suffering from infection of the lungs; and that nearly all glandular enlargements in individuals dying from causes other than tuberculosis were found to be tuberculous. These facts, together with the large mass of research in tubercular infections throughout the world seem to leave no room for doubt that such three stages of the infection exist and that tuberculosis of the glands is the primary form of the infection. We see case after case of tuberculosis of the glands of the neck followed by tuberculosis of the bone and if double infection occurs in

Tuberculosis, like syphilis, may be considered in three stages: the glandular stage, the bone and joint stage, and the pulmonary stage. Figs. 13 & 14.

FIG. 13.—ILLUSTRATES THE THREE STAGES IN ONE INDIVIDUAL, GLANDS; BONE (sternoclavicular joint and sternum); LUNGS.

This patient, a Chinaman, twenty-five years old, has had suppuration of the glands of the neck since early childhood. Several operations, two of them radical, were performed, but each time the wound failed to close. About two years ago, and directly after the last operation, the disease extended to the sternoclavicular joints on both sides. A cough developed which lasted for two years. On examination, both lungs were very extensively involved. He disappeared from the clinic after a few visits. We subsequently learned that he was discouraged from taking tuberculin treatment by other physicians (as if there was any chance for recovery by any other treatment).

FIG. 14.—ILLUSTRATES THE THREE STAGES IN A CHILD, GLANDS (neck and mediastinal); BONES (both hips); PULMONARY.

This photograph represents a more rapid progress of the disease, where little natural resistance could be developed during the spread from one stage of the disease to the other.

a very young child, it finally dies of an extension into the lungs. In older individuals, the process will remain in the bone or joint, the glands perhaps showing a tendency to heal. The process then becomes very chronic, the resistance of the patient being sufficient to prevent an extension into the lungs, but not quite sufficient to put an end to the infection.

It therefore follows, that since tuberculosis of the glands represents the primary lesion, it offers an ideal situation for the checking of the infection, and this should be our main aim. The removal of the hypersusceptibility by a course of tuberculin will remove the probability of an extension of the disease.

Since the glandular form of the disease represents the primary infection it offers the ideal situation for immunotherapy.

The healing of the local lesion is by far less important. Too much attention has been paid to the local condition in glandular tuberculosis and the efficacy of tuberculin treatment in tubercular glands was judged by the course of the local process during the treatment. The success of tuberculin thus depended upon the presence or absence of coexisting processes other than the tubercular affection; for we know that many processes can supervene upon a tubercular process which may remain after successful treatment was directed against the tubercular process alone. If, on the other hand, we remember the greater responsibility,—that of checking an infection which is in its primary stage,—and give our attention to the local condition secondarily, the great utility of tuberculin in tubercular infections would become apparent to every one.

We are dealing with a constitutional disease, its local manifestations should receive only secondary consideration.

The radical surgical operation is a severe incursion upon the already delicately balanced organism and the recurrence is due to the tubercle bacillus left behind, not on account of the lack of surgical skill, but because of the presence of the tubercle bacilli which are beyond the reach of the knife. The organism thus rendered more susceptible allows of a greater spread of the disease than before the operation, for the hypersusceptibility is greatly increased by any surgical interference requiring a general anesthesia.

The radical operation is a failure for the reason that it deals with the local conditions alone, and may do great harm by reducing the natural resistance of the patient.

Classification. A more detailed classification with regard to the pathological processes involved in tubercular glands will greatly simplify the whole matter and will render much clearer the differentiation between the tubercular process and other pathological processes that may supervene. Once such differentiation is made, we shall know on the one hand what to expect of the tuberculin and we shall recognize, on the other hand, the necessity for other therapeutic measures when they are indicated.

Closed Glands

Closed tubercular glands consist of two varieties, the hyperplastic glands which undergo caseation and softening

Under this heading, we class all tubercular glands that are enlarged, but have not broken down. They remain as masses of various sizes with a process that is purely tubercular. Consequently, we have two varieties of closed glands each dependent upon one of the other of the two varieties of processes that tuberculosis gives rise to; that is, hyperplastic and fibrous. To the hyperplastic variety belong the glands where the glandular substance increases together with infiltration of the stroma, causing poor blood supply to the center of the gland. The center of the gland soon liquefies and finally forms a cold abscess, or soft gland. It may remain soft for a long time. If left alone, the soft gland will finally acquire a tryptic ferment which will digest its capsule, finally eating its way out to the surface and produce very ugly scarring. This process resembles a sloughing process. It is therefore necessary at the outset to aspirate these glands and treat them as described in Part III, under "Surgical Treatment."

and

the fibrous glands with scar tissue formation.

The fibrous glands are those in which the individual has a fair amount of resistance and reacts to the tubercular process by fibrous tissue degeneration. The longer the process goes on, the denser becomes the fibrous tissue in these glands so that when a course of tuberculin has checked the tubercular infection, this fibrous tissue will contract to a greater or lesser extent as a result of complete healing. Since fibrous

FIG. 15.—ILLUSTRATES THE FIRST AND SECOND STAGE—GLANDS OF THE NECK AND BONE.

This patient, fifty-four years of age, has been suffering from the glandular and bone infection for fifty-one years. The spread from the glands in the neck to the bones and joints was very rapid, but here the progress remained very slow and although the disease spread from one joint to another, there was sufficient resistance to prevent the spread into the lungs.

tissue does not entirely absorb, it will very frequently leave a hard nodule, the size of which depends upon the number of glands involved. (Fig. 16.)

One can readily see the fallacy in the conclusion that tuberculin has not cured the patient if such a nodule persists But a slight experience is needed with the radical operation for the removal of these glands to appreciate the difference between an operation such as would be required before tuberculin had been administered and one that would be sufficient to merely remove the cicatrized glands after tuberculin had been administered. (Fig. 17.)

Open Glands.

By open glands we mean glands that suppurated to the surface. They are of two distinct varieties. Those that have broken down as a result of tryptic ferments, the discharge of which is sterile; and those that have broken down through suppuration due to a mixed infection. Of the latter, there are two varieties: the suppurating hyperplastic variety (Figs. 6 and 7) and the suppurating fibrous variety. In the process of healing during a course of tuberculin, no difficulties will be met with in the case of any of the open glands, except with the fibrous suppurating variety. While it may happen that the mixed infection goes on to destroy all of the fibrous tissue, this is not usually the case. A large amount of fibrous tissue will remain after both the tubercular and the mixed infection have been checked, so that here again we have a case where surgical interference may be necessary to complete "a cure." (See Part III.)

Open glands are of two varieties: (a) those broken down by tryptic ferments; (b) those broken down by mixed infection.

Of the second, (b), there are two varieties: (1) suppurating hyperplastic; (2) suppurating fibrous.

Recurrent Glands After Radical Operation.

(Figs. 8 and 9.)

A recurrence after radical operation may take place immediately after the operation, preventing primary healing of the incision; the sutures break apart and a large

Post operative recurrent glands are of two varieties:

(a) Those recurring immediately after operation consisting mainly of mixed infection;

suppurating area forms, with a mass of enlarged glands beneath it. The rapidity with which the glands enlarge, from an invisible size to a mass almost as large as previous to the operation, implies mixed infection, for the tubercular process alone can not cause such rapid enlargement, However, the increased hypersusceptibility is a factor in the recurrence. These patients will very often run high temperatures and show marked symptoms of toxemia. The treatment of the mixed infection as described in Part III of this work, must be persisted in until the temperature is reduced before tuberculin inoculations are begun.

(b) Those coming on slowly and some time after the operation.

Another form consists of a recurrence some time after a seemingly successful operation. These glands, as a rule, come on more slowly, are of a purely tubercular character and should be treated as closed glands, taking into account the heightened susceptibility. This increased hypersusceptibility may persist no matter how long an interval has elapsed between the operation and the tuberculin treatment. Glands enlarged through a tubercular process on the opposite side of the neck or anywhere else in the body should be treated the same as recurrent glands, if they appear after a radical operation; that is, we must take into account the heightened susceptibility due to the operation, no matter whether the process is recurrent or newly formed. (Fig. 20.)

General Hypersusceptibility

Three grades of hypersusceptibility exist in tubercular adentitis.

We have three distinct grades of general hypersusceptibility to deal with in tubercular lymphomata. The closed glands represent the lowest grade of hypersusceptibility. That is easily explained when we recall that the glands in the body are the filters and detain the infectious organisms on their way to the more vital organs. That is also the reason why glandular tuberculosis represents the primary infection with the tubercle bacillus. It therefore follows that so long as the glands remain closed, they are successfully coping with the infectious organisms, although they are undergoing pathological changes as a result. As soon

as these glands break down, they no longer serve as filters. extension of the process becomes more likely and thus represents a heightened susceptibility. The third grade of hypersusceptibility occurs in glands that appear as an active process in spite of and following a radical operation.

There is one exception to the general rule of hypersusceptibility in tubercular glands, and that is: after an infectious disease the hypersusceptibility is very high in any form of tubercular glands, even in case of the closed form. This increase in hypersusceptibility bears no relation to the severity of the infectious disease, as we may have a much larger increase in hypersusceptibility after a mild attack of grippe or varicella than after a severe scarlet fever. However, we must remember that an increase in hypersusceptibility does occur and must be taken account of if tuberculin treatment is resorted to before six months have elapsed. We have all noticed the frequency with which tubercular processes in children first make their appearance after a contagious disease. That is most likely due to heightened susceptibility as a result of the infectious disease, rendering a quiescent lesion active. (See Temperature Charts, page 151, 152.)

Contagious diseases increase the hypersusceptibility to a marked degree.

Beginning Treatment.

From the above, it follows that in the treatment of closed tubercular glands, 0.0001 c.c. of tuberculin or 0.10 c.c. of the third dilution would not be too large a beginning dose. In the open tubercular glands, 0.00001 c.c. or 0.10 c.c. of the fourth dilution would be less likely to give a reaction from the first dose. In cases following a radical operation, 0.000001 c.c of tuberculin or 0.10 c.c of the fifth dilution should be the beginning dose if the recurrence appears immediately after the operation. If the recurrence does not appear until some time after the operation and the patient seems in good physical condition, 0.00001 c.c. or 0.10 c.c of the fourth dilution should be the beginning dose. The same holds true in tubercular glands

The beginning dose of tuberculin.

if the treatment is begun before the elapse of six months after contagious disease, when 0.000001 c.c. or 0.10 c.c. of the fifth dilution is a safe dose to begin with. Occasionally the hypersusceptibility is so marked as evidenced by a daily temperature rise and by a marked irritability of the patient, that the sixth dilution should be made and the treatment begun with a 0.10 c.c. making the beginning dose 0.0000001 c.c. of tuberculin. In the treatment of Orientals or negroes, one-tenth the quantity advised as beginning treatment above should be the beginning dose under similar conditions.

Conclusion of Treatment.

The conclusion of treatment.

In glandular tuberculosis, it is rarely necessary to conclude the tuberculin treatment in any way other than is shown on the general scheme of dosage, as described in the last chapter. After the administration of the BE the patient returns every three months for test inoculation to determine whether there is a tendency for the return of hypersusceptibility. The method of testing will be described more fully under its own heading. (See page 147.)

Results.

The results in glands have been universally good where tuberculin has been adopted.

The results obtained from the treatment of tubercular glands with tuberculin leave no doubt that tuberculin is the treatment par excellence for this condition. Among others the late Doctor John B. Murphy, of Chicago, found that in a number of years no case of glands of the neck required operation where a course of tuberculin had first been given.

That the radical operation is contra-indicated in every case of tubercular glands is beyond dispute. Those that still resort to the radical operation will find the responsibility harder to shoulder with the ever increasing recognition of the fact that glands can be cured without it. There are those who deny that tuberculin will cure all cases of glands. This denial may be based upon the expectation that tuberculin should not only cure the infection, but must eradicate every

sign of the disease. Many have "tried" tuberculin and have discontinued every other treatment. And when tuberculin failed to remove a mixed infection, or when tuberculin eradicated the tubercular infection but left behind a mass of fibrous tissues which could not be absorbed, these masses were pointed out as the original glands and it was declared that tuberculin had failed in its therapeutic effects. Granting that a surgeon honestly believes that glands enlarged through tuberculosis ought to be removed,—he ought even then to take cognizance of the fact that tuberculosis is a systemic disease and ought in every case rid the system of the hypersusceptibility before resorting to surgery for the local condition. If this fact were always considered, the whole problem would automatically adjust itself to all forms of opinion. For, the surgeon would observe the large number of patients who get well without operation. He would also notice that when an operation is performed after tuberculin, the fact that no recurrence takes place would more than emphasize the advisability of a course of tuberculin before operation.

The radical operation for tubercular glands is contra-indicated under all circumstances as tuberculin, if it does not remove all traces of glands, will at least limit surgical interference to the removal of a cicatrized mass which could not be absorbed.

In hospital, as well as in private practice, I have had uniformly good results with tuberculin in the treatment of glandular tuberculosis. In only two cases was an operation necessary and both these cases were post-operative recurrent glands. One patient (Fig. 17) had had a radical operation for cervical adenitis, with recurrence in the submaxillary region. Applying for treatment about four months after the radical operation, we found the incision for the radical operation extended from the tip of the mastoid to two inches above the clavicle, then at right angles across the neck to the sterno-clavicular joint. The lower half of the horizontal incision was suppurating and consisted of a large granulating surface. She also presented a very high grade of hypersusceptibility with a mass in the submaxillary region the size of a hen's egg on the same side where the operation was performed. This mass, during treatment, reduced to the size of a walnut, but persisted after the conclusion of the course

of tuberculin. Under local cocain anesthesia and through a half-inch incision, the mass was removed, the incision closing by primary union, leaving an almost invisible scar. The removed mass consisted of a very dense fibrous tissue with hardly a vestige of glandular substance to be seen. During the tuberculin treatment, the patient gained twenty pounds in weight, and lost the nervous irritability and tremor of the hands which she had when she first presented herself for treatment.

The second case, a woman twenty-nine years of age, with a negative family history, was always well before the present complaint and did not remember any diseases of childhood.

At the age of fifteen, the glands of the neck on both sides began to swell; and until six years ago, the swelling continued, sometimes in a milder form, sometimes very marked, at times almost disappearing on one side and then on the other, but at no time was she free from enlargement of the glands of the neck.

Six years ago she suddenly developed a painful enlargement of her whole abdomen, the pain being specially marked in walking and from any jar whatsoever. About a month later, an exploratory laparotomy was performed and extensive tubercular peritonitis was discovered. Thirty ounces of fluid were removed and the peritoneal cavity exposed to the air and sunlight for "one hour." Nine days after this operation the abdominal cavity refilled, and after remaining confined to her bed for six weeks she was sent to a sanitarium in the mountains where she improved, the fluid disappearing from the abdomen after a period of six months.

One year later, the glands of the neck, which were of the closed variety up to the present time, began to suppurate, especially the sublingual mass. Under a general anesthesia and through an incision extending from the angle of the lower jaw on one side to the same point on the other side a complete removal of this mass of suppurating glands was thought to have been carried out, but soon after the operation the mass recurred, and the incision suppurated at several

points. A month or two later, another radical procedure was carried out over a suppurating supraclavicular mass on the right side, with no better result; and during the year following, six more general anesthesias were administered to the patient for the removal of one mass after another in both the cervical regions on both sides of the neck the supraclavicular region on the left side, and in the suprasternal region. The posterior cervical chains suppurated on both sides but no attempt for their removal was made. Soon after the last operation on the neck, and two years after the first abdominal operation, the upper right abdomen began to swell and in the course of the following few weeks two large abdominal abscesses were opened and drained. These abscesses did not penetrate into the abdominal cavity and healed in a few weeks. About eight months later, an acute swelling of the abdomen again occurred with symptoms of peritonitis, such as abdominal rigidity, nausea and vomiting. Laparotomy was performed through the former median incision. A suppurating appendix was removed and a number of tubercular masses were found and removed. The patient recovered from this operation, but suppuration of the incision occurred with the formation of a fecal fistula. Soon after this operation, a large mass of glands in the right axilla developed which suppurated a few months later. The patient applied for tuberculin treatment several months after the last abdominal operation (March 30, 1914). She weighed 130 pounds although she is five feet eight inches tall, was very pale, and highly neurotic. Around the neck, including both supraclavicular and suprasternal regions, the anterior and posterior cervical and the sublingual regions were studded with openings from suppurating glands (about fifteen in all), oozing a thick creamy pus. The lower jaw gave the appearance of acromegaly from the distortion brought about by the enlargement of the submaxillary and sublingual glands. The abdominal wall showed two longitudinal scars in the upper left quadrant and a median scar running from the umbilicus to the symphasis pubic. In the lower part of

the median scar and about one-half inch above the symphasis there was a fistulous opening from which oozed a thick creamy pus, and after physic had been taken this would discharge feces. The tuberculin treatment continued uninterruptedly until April 9, 1915, and except for a few mild constitutional reactions and a number of severe local reactions the patient improved steadily, weighing 180 pounds at this time. Five masses persisted beyond this treatment, three on the left side and two on the right side of the neck. The two masses on the right side were removed under cocain anesthesia with primary union. In August, 1916, I performed an operation for the relief of the fecal fistula, and at the same time removed one more mass on the left side of the neck. Outside of tuberculin, a vaccine for mixed infection was administered during her treatment, and just before the operation for the removal of the fecal fistula, three prophylactic inoculations of strepto-fecalis and colon bacillus were administered a week apart:

First dose strepto-fecalis 250 mil. Colon bacillus 250 mil.

Second dose strepto-fecalis 500 mil. Colon bacillus 500 mil.

Third dose strepto-fecalis 1000 mil. Colon bacillus 1000 mil.

The important points to be noted in this case are:

1. The rapid extension of the tubercular process to all the glands of the neck and their final breaking down did not take place until after a major surgical operation (laparotomy) was performed although the glands were diseased for many years before.
2. The tubercular affection of the glands is only a local manifestation of a constitutional disease. The attempted extensive operation for the relief of the local process only lowered the resistance of the patient, allowing the disease to get a firmer hold on the constitution, which manifested itself at some point of lessened resistance—most often at the point of operation and sometimes in more

vital organs which happened to be in a state of lowered resistance.

3. Masses of fibrous tissue may become foreign tumors after the infection (disease) has been eradicated, and may require removal.
4. The removal of these masses is infinitely simpler and safer after the constitutional disease has been overcome.
5. Although at the first two laparotomies, extensive tubercular peritonitis was found, there was no sign of peritoneal involvement found at the laparotomy for the cure of the fecal fistula performed after the tuberculin treatment.
6. Prophylactic immunization with stock vaccine of bacteria found by a bacteriological examination of the fistulous discharge made a cure by one operation possible. (See Part III.)

In both these above cases it will be seen how much more effective surgery is when applied in a condition that is purely local than in a similar condition when the local manifestation is still a manifestation of a systemic condition. With Petruschky and Kramer, I hold that tuberculin will effect a cure in 100 per cent. of cases. From extensive experience in recurrent cases after radical operation, I maintain that the radical operation cannot be justified in any case; and in a child under five years of age, it is criminal; for, in those cases a resistance has not been built up to any degree and a general dissemination is very imminent. The following is a case to illustrate this point.

Tuberculin is effective in 100 per cent of cases of adenitis.

Willie R., born in September, 1913, whose family history was negative, had a normal birth and was always well. On September 1, 1914, a swelling was noticed on the left side of his neck. This grew larger until November 20th, when a radical operation for the removal of tubercular glands was resorted to, the incision extending for three inches along the inner border of the sternocleidomastoid muscle. The wound reopened soon after the operation, forming a granulating sur-

face occupying nearly the entire side of the neck. When the child was brought under my care on February 10, 1915, his temperature ranged for a week previous between 101° F. and 105° F. daily, the wound in the neck consisted of an oval depression about two and one-half inches long and one-half inch wide, with the edges composed of thick granulating tissue. From the center of the wound oozed a thick creamy pus. A chain of enlarged glands ran parallel to the outer border of the sternocleidomastoid muscle with one enlarged gland beneath the lower angle of the wound. Already a tendency for the dissemination of the tubercular process made itself evident by the appearance of two distinct lupus spots on the shoulder and chest. I did not seek to clear the mixed infection by vaccine before beginning with the tuberculin treatment, owing to the tendency for the dissemination of the tubercular process and the length of time that the mixed infection had persisted (nearly three months).

I have here inserted a chart showing nearly the entire course of treatment in this case. I did so because of several other important points which the case illustrates and which come up in the treatment of children.

Child R. Age 17 mos., male, diagnosis—tubercular adenitis.
1915

Date	No.	No. Dil.	Quant. per c. c.	Reaction Local	Reaction Temp.	Wgt.
Feb. 15	1	IV	0.10*	0	104.5	20 lbs.
19	2	"	0.12*	0	103.8	
22	3	"	0.16*	0	103	
25	4	"	0.22*	+++†·	103.6	.....
Mar. 5	5	"	0.10	0	102.8	
9	6	"	0.12	0	101.4	
14	7	"	0.14	0	100.4	
21	8	"	0.18	0	100	

* To hasten the treatment the increase was increased at every inoculation.

†The distinct local reaction indicates that the slightly greater rise in temperature is a constitutional reaction.

FIG. 16.—AN EXAMPLE OF HARD CICATRIZED GLANDS AFTER CONNECTIVE TISSUE CHANGE.

This scar is the result of an operation for the removal of a large mass of glands in the supraclavicular region. The patient applied for treatment six months after the operation on account of the failure of the wound to close. It had formed a wide granulating surface, and had the appearance of a mass of glands in the cervical region.

The patient is still under treatment. Both the operation and the fact that she is Italian are responsible for a very high degree of hypersusceptibility, which is making the tuberculin treatment unusually prolonged in her case, although the wound promptly closed after a few weeks of treatment. These glands cannot completely absorb, not on account of any deficiency in the therapeutic value of tuberculin, but because cicatrized connective tissue rarely absorbs. After the hypersusceptibility is removed by tuberculin, a small incision will be sufficient to remove the mass of cicatrized glands. The healing of the incision by primary union will be no less assured than in the case of any other non-infectious operation.

FIG. 17.—SHOWS THE DIFFERENCE BETWEEN A RADICAL OPERATION BEFORE TUBERCULIN TREATMENT AND A COSMETIC OPERATION AFTER TUBERCULIN TREATMENT.

The scar was very prominent when the patient first presented herself for treatment at the New York Polyclinic Hospital, four months after the radical operation performed elsewhere. The angle of the scar was suppurating at the time. In order to show the extent of the incision for the radical operation it had to be painted with iodine just before this photograph was taken, so much has the scar absorbed during the tuberculin treatment.

This photograph illustrates another bad feature of the radical operation, especially when the chain of glands extends over the region of the spinal accessory nerve. Evidently the nerve was injured during the operation with the resulting dropped shoulder. The nerve supply to the deltoid muscle was also injured as there is very limited motion to the shoulder with considerable atrophy. The scar resulting from the removal of the submaxillary gland is barely visible.

FIG. 18.—OPEN TUBERCULAR GLANDS—CAN A RADICAL OPERATION CURE THIS PATIENT?

The tubercular process is not only in the suprasternal, supraclavicular and anterior cervical glands but in the superficial chain along the inferior border of the lower jaw from the right ear lobe to the chin, also involving the submaxillary gland on that side.

Because of a very high degree of hypersensitiveness the treatment of this patient was very long drawn out.

FIG. 19.—OPEN TUBERCULAR GLANDS—CAN A RADICAL OPERATION CURE THIS PATIENT?

Following an operation for the removal of a mass of tubercular glands in the right axilla, extensive suppuration took place in the incision, soon followed by the appearance of tubercular glands in the neck, as shown in this illustration.

The susceptibility at the commencement of treatment was very high, rendering the treatment longer than usual.

Fig. 20.—Illustrates a Radical Operation With Extensive Recurrence a Few Months After the Operation.

FIG. 21.—ILLUSTRATES A RADICAL OPERATION WITH IMMEDIATE RECURRENCE, WITH THE EXTENSION OF THE PROCESS TO THE APEX OF THE LUNG.

FIG. 22

The patient, a young man thirty years of age, born in the United States, a clerk by occupation, had a maternal uncle who died of pulmonary tuberculosis. In his childhood he lived with this uncle during the active stage of the disease. He had measles and whooping-cough in early childhood, and outside of frequent sore throats, was well until his sixteenth year. Fourteen years ago, he noticed that the glands on the right side of his neck (cervical region) began to swell. In six months they grew to such size that an operation was advised, and performed under a general anesthesia. One week after this operation, the wound suppurated, swellings appeared in the parotid region in the supraclavicular region, and in the entire posterior, cervical chain. These all broke down, so that after five months of invalidism, another operation was declared necessary, and performed under a two-hour general anesthesia. The patient stated that the surgeons declared "that it was necessary to go down to the jugular vein and to the lung in order to remove all traces of the disease." A month after this operation, four or five "lumps" appeared on the same side in the posterior cervical region, which he carried for five years, being unable all that time to wear a collar on account of their awkward position and the sentitiveness of the scars. Seven years ago, these swellings suddenly began to suppurate. An operation was again performed under general anesthesia. Three days after this operation, the whole wound broke open with a great deal of sloughing of tissues. The patient declared that for three months "the hole in the side of his neck was large enough to admit a fist." After a great deal of local treatment lasting over a period of nine months the wound finally granulated and closed. Fig. 10 shows the extensive scarring of the side of the neck which was the seat of the tubercular process up to the present.

In June, 1916, or five months before the patient was referred to me for tuberculin treatment, he noticed that the right side of his neck was rapidly swelling, becoming steadily larger until the mass occupied the entire side of his neck as shown in Fig. 23. Treatment was commenced at once. And although these glands were closed, I began with the fourth dilution on account of the previous radical operations. He ran a slight temperature when he first started, going up to 99.4° F. by mouth every afternoon. There were several local reactions after the first few treatments. After the eighth inoculation, he had his first constitutional reaction, in which the temperature rose to 100° F., the local reaction being at the same time quite severe and the constitutional symptoms being very definite.

Both the local reactions and the constitutional reaction have greatly retarded his tuberculin treatment; but it is not the quantity of tuberculin nor the frequency of inoculations that influence the therapeutic effects of tuberculin; it is the proximity of the dose to the maximum tolerance that makes it most effective. Fig. 24 shows the same young man barely four months after the beginning of the tuberculin treatment. The swelling in his neck has entirely disappeared, he is gaining in weight, and he has returned to his occupation which he is now able to pursue without interruption.

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FIG. 22.—POST-OPERATIVE RECURRENT GLANDS.

This case illustrates the futility of any operation which aims to remove the local manifestations of a constitutional disease. (See pages 83 and 84).

FIG. 23.—POST-OPERATIVE RECURRENT GLANDS.

The right side of the neck of same patient as Fig, 22 when tuberculin treatment was commenced.

Mar.	25	9	IV	0.22	0	100.2	
	29	10	"	0.28	+	‡	22.5 lbs.
Apr.	5	11	"	0.28	+++	102.2‖	
	12	12	"	0.18	0	100	
	16	13	"	0.20	0	100.4	
	19	14	"	0.22	++	101.8	
	26	15	"	0.14	0	Normal	
May	3	16	"	0.16	0	"	
	7	17	"	0.18	0	"	
	10	18	"	0.20	++	"	23.5 lbs.
	17	19	"	0.24	+	"	
	24	20	"	0.28	+	"	
	31	21	"	0.34	++	"	
June	7	22	"	0.40	0	"	
	11	23	"	0.50¶	++	102.4	.....
	19	24	"	0.34	0	Normal	
	22	25	"	0.36	0	"	
	26	26	"	0.38	0	"	
	30	27	"	0.42	0	"	
July	6	28	"	0.46	0	"	25.5 lbs.

NOTE 1. The first four inoculations represent an increase of the increase at every inoculation instead of at every other inoculation. I did this in order to reach the maximum of tolerance as soon as possible having begun with the fourth dilution, because it was a post-operative case. I felt that if the hypersusceptibility happened not to be increased by the operation there would be an unnecessary delay in reaching the maximum tolerance. A distinct reaction after the fourth inoculation pointed to the fact that the beginning of treatment with the fourth dilution was correct in this case, and that from the start I was fairly near the maximum of the child's tolerance. That explained the rapid drop in temperature from the very beginning of treatment. The reason why I considered 103.6° F. as a distinct constitutional reaction was the fact that there was a severe local reaction accompanying the rise in temperature of 0.6 of a degree higher than the maximum temperature for three or four days previous to this increase.

‡Temperature record neglected but slight local reaction present, hence, dose not increased.

‖Temperature reaction after this inoculation proves that a reaction had occurred after last dose.

¶This dose should have been 0.45 c.c. which might have avoided the reaction.

lation. If there were no local reaction at the point of inoculation on the arm, even a much higher rise would not be considered a constitutional reaction, but would be attributed to a larger amount of absorption from the wound area or to some intestinal derangement, etc., occurrences which are so frequent in children at that age.

Analysis of the tenth inoculation which was given on the 29th of March, illustrates a common occurrence in the treatment of children where the mother has all the household duties and the care of the patient on her own hands. When the mother brought the child on April 5th, I found a mild reaction as represented by one plus (+) from the previous inoculation, the mother reporting that she was too busy to take temperatures. I therefore repeated the same dose on the 5th of April that I gave on the 29th of March for this reason: with a local reaction present, there might or might not have been a constitutional reaction, after the previous inoculation. If there was a constitutional reaction, the same dose will produce a constitutional reaction again. The second constitutional reaction may be slightly more severe, but will avoid too great a drop in the dose in case it was found that no reaction had occurred. In this case, there was a severe local reaction and a moderate constitutional reaction, proving that the dose previous had also produced a reaction. But if the eleventh inoculation had not produced a reaction, there would have been a loss of one inoculation, whereas, if we had not made this test and the eleventh inoculation would have been 0.18 we would have lost nearly one month of treatment before the maximum would again have been reached. It is always advisable in case of a doubtful constitutional reaction to repeat the last dose before reducing the amount of tuberculin.

After the fourteenth dose, on April 19, there was a rise in temperature to 101° F. which I considered a distinct reaction on account of the local reaction present. Owing to the fact that this reaction occurred so soon after the last one, a larger reduction in dose than usual was made; that is, I reduced the dose to the amount to which it would have been reduced had the reaction occurred after the first time 0.22 c.c. had been administered, as at the ninth inoculation. Subsequently, and for the same reason, I increased, by 0.02, the three following inoculations instead of only two, and after the eighteenth inoculation, continued in the usual manner. However, on account of the local reactions, occurring four times in succession after the eighteenth dose, the inoculations could be given only once a week. After the twenty-third inoculation, there was a distinct constitutional reaction occurring as a result of an error in the amount of the increase. There should have been an increase of 0.08 c.c. instead of 0.10 c.c. Although the rise of temperature was to 102.4° F. the constitutional symptoms were mild, the rise in temperature in a child at that age being usually out of proportion to the cause. The usual indications were followed; that is, after a wait of a full week, the treatment was resumed with an amount of tuberculin equal to the third last inoculation with the increases from there on as at the beginning of the treatment.

From the end of April, the wound began to contract and the discharge diminished day by day until the beginning of June, when the wound closed completely. After the inoculation of June 11, it discharged slightly from the upper angle but soon closed again and never reopened.

The treatment was continued without any further interruption until the end of November, at which time no trace of disease remained, except the linear scar marking the place of the operation. It may be noted that my original conclusions as to the mixed infection were correct. The wound was so shallow that with the disappearance of the tubercular process, the consequent improvement of the general health was sufficient to overcome the mixed infection.

The following case illustrates the futility of any operation which aims to remove the local manifestations of a constitutional disease.

The patient, a young man thirty years of age, born in the United States, a clerk by occupation, had a maternal uncle who died of pulmonary tuberculosis. In his childhood he lived with this uncle during the active stage of the disease. He had measles and whooping-cough in early childhood, and outside of frequent sore throats, was well until his sixteenth year. Fourteen years ago, he noticed that the glands on the right side of his neck (cervical region) began to swell. In six months they grew to such size that an operation was advised, and performed under a general anesthesia. One week after this operation, the wound suppurated, swellings appeared in the parotid region in the supraclavicular region, and in the entire posterior, cervical chain. These all broke down so that after five months of invalidism, another operation was declared necessary, and performed under a two-hour general anesthesia. The patient stated that the surgeons declared "that it was necessary to go down to the jugular vein and to the lung in order to remove all traces of the disease." A month after this operation, four or five "lumps" appeared on the same side in the posterior cervical region, which remained for five years. He was unable all that time to wear a collar on account of their awkward position and the sensitiveness of the scars. Seven years ago, these swellings suddenly began to suppurate. An operation was again performed under general anesthesia. Three days

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FIG. 24.—POST-OPERATIVE RECURRENT GLANDS.

The right side of the neck of same patient as Fig. 22 four months after tuberculin treatment has been administered.

[redacted]

Chapter IV

BONE AND JOINT TUBERCULOSIS

The subject of bone and joint tuberculosis stands next in importance to pulmonary tuberculosis. And that only as regards the number of cases afflicted, for it stands second to none in the gravity of the problem it presents. Attacking as it does its victims in childhood and early adolescence, it at once affects the individual as to his entire future existence, no matter how mild a course the disease may run. On the one hand, it prevents the proper fundamental education which one can acquire only at that age; and on the other hand, it disorganizes his physical makeup, interfering with or even preventing any occupation which would keep him from becoming a burden on society. There is nothing so much the subject of pity as a cripple, no matter what the cause may be. But when added to the deformity we have invalidism, as in a case of tuberculosis of the joint, it is lamentable. A physically deformed individual in the course of years becomes accustomed to the deformity and with the finding of an occupation that has become suited to his condition, may even learn to enjoy the pleasures of life with but an occasional sting coming from the consciousness of his being deformed. But when this deformity is caused by tuberculosis, especially open tuberculosis, with discharging sinuses, the gradual diversion of the mind towards the ordinary pursuits is prevented by the necessity of constantly nursing his wounds and by the pain and discomforts which confine him to his bed or to limited activity beyond it.

Although pulmonary tuberculosis counts a great many more victims, bone and joint tuberculosis offers no less a problem both with regard to the effect of the disease on the victim, and with regard to the status of the victims in the community.

In its progress, medical science seems to have overlooked this pitiful army of suffering children. The best proof that the profession seems to have abandoned these unfortunates as hopeless, is the tendency to convert hospitals for tuberculosis cripples to "homes" for crippled

children, with the establishment of educational systems. The name "home" to signify the permanency of residence and the institution of the educational system has come in answer to the law requiring universal education. Fortunately it also serves the greater purpose of occupying the minds of these sufferers for at least part of the day and of diverting them from their miseries.

Up to the present time these "homes" can only accommodate a small fraction of the victims.

The number of children taken care of in "homes" is insignificant in comparison with the great army of crippled children throughout the land, who are unable to get accommodations in such "homes." And if the lot of those in the "homes" and hospitals is so pitiful, what can be the lot of those children who are kept in the homes of the poor? How much care and attention can a crippled child get in the home, where the burden of the care of a number of other children falls upon the mother in addition to the care of the home, and where even the support of the family frequently falls to her lot?

In the case of bone and joint tuberculosis, an efficient remedy would be welcomed almost as enthusiastically as one for pulmonary tuberculosis. What then has prevented the wider adoption of tuberculin in the treatment of bone and joint tuberculosis? With the brilliant results obtained by the use of bismuth paste, as reported by Beck, constantly before us, why has it not been more widely adopted by the medical profession? No one can doubt the efficiency of Bier's hyperemia in tuberculosis of the bones and joints; nor can we question the veracity of its author's reports of his success in a large number of cases. Why have we not adopted this method more generally in the treatment of the bone and joint condition? Favorable reports from the use of vaccines in discharging sinuses are coming from unquestionable sources, especially from England. What is the reason that we are so slow in adopting the vaccine treatment of these conditions?

There is but one answer to all these questions and that

is: That in attempting the use of any one of these methods, we have neglected to study its mode of action and have looked upon it in the nature of a "cure-all." We have so far failed most hopelessly in the recognition of the multiplicity of processes that constitute a joint tuberculosis with discharging sinuses. We know that the underlying cause is the tubercle bacilli but the condition ceases to be a purely tubercular inflammation as soon as there is destruction of the joint lining, with affection of the bone substance. We have now to deal with a changed structure, which has its bearing upon the mechanism of the joint involved and which is quite apart from the tubercular process. In other words, any agent, however marvelous in its action, if it were to remove the affection completely and at once, would still leave the problem of deformity unsolved. Is it just to condemn such a therapeutic agent, because in removing the infection it failed to restore the function of the joint? And still that is just what is being done in failing to adopt any one of the above mentioned methods of dealing with tubercular joints or bones; and so long as we persist in discarding all therapeutic measures which do not accomplish a complete cure all at once, so long will we fail in our treatment of these cripples. Such a therapeutic agent will never be discovered, for it aims at the accomplishment of diversely different objects. But on the other hand, if we recognize the complexity of the processes involved, and the nature of each of these processes, we shall realize at once how near at hand is the complete cure of nearly every case.

The profession has overlooked the multiplicity of processes involved in bone tuberculosis.

The elements going into the formation of tuberculosis of the bones are:

Let us consider the various processes involved in tuberculosis of a joint. First and foremost, we have anemia of the part involved. This anemia is responsible in most part for the chronicity of the process and nothing that requires the circulatory system for its therapeutic effect can be of any value unless this is corrected. Hence, in this condition, tuberculin depends for its favorable effect upon the focal

1. *Anemia.*— The disease of bone does not carry with it a natural hyperemia as does disease of other tissue.

hyperemia that it produces far more than upon the immune response it calls forth. (See Fig. 25.) It may be that the patient already has sufficient immune response and the failure of the circulation to bring the products of this response to the point of infection has been responsible for the progress of the disease. So it happens that Bier's hyperemia has cured a great many of these cases, by increasing the circulation in the affected joint and permitting the patient's own antibodies to get to the point of the infection.

2. *Mixed infection.*— This may continue a local process after the causative has been element removed.

Mixed infection is responsible for the continuation of the local condition over a period of years, even though the tubercular process itself has long since disappeared from the local condition. Therefore in cases where the mixed infection is the predominant process vaccines have proved successful. (See Fig. 14.)

3. *Serous accumulations.*— By being the best of culture media the growth of bacteria is constantly encouraged beyond the reach of the defensive mechanism of the afflicted.

Long sinuses and bone cavities will heal irregularly when they show a tendency to heal, enclosing infected material between the healed areas which may stay quiescent for a while, but finally must get an outlet and therefore suppurate,—producing a recurrence of what was supposedly a cured case. This represents a condition where the infection being tubercular, or mixed, has ceased to be a factor in the continuation of the process. The accumulation of irritating materials in these cavities and sinuses continues their existence. Filling these sinuses and cavities with bismuth paste prevents such accumulation and at the same time causes a universal contraction of tissues upon this foreign substance, producing complete healing. But even Beck warns against the use of bismuth paste where there is an active inflammatory process present; for here the main cause of the condition is a virulent bacteria, and not the mechanical structure.

4. *Irregular healing.*— When spontaneous healing once sets in, it does so irregularly, causing the encysting of irritating inflammatory discharges cause which finally recurrence.

The placing of an early infected joint at rest will make a spontaneous cure possible wherever there is a tendency for such a cure, hence many of these patients have been cured by orthopedic appliances alone.

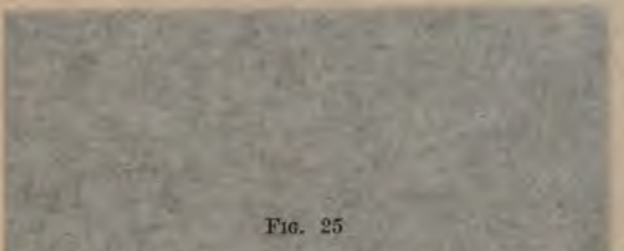

FIG. 25

The amputation in this case was not an operation for an emergency. Would it not have been more rational to have localized the lesion by a course of tuberculin treatment before the amputation? That tuberculin would have localized the lesion in this case is beyond doubt, for it has since demonstrated its ability to do so in this case.

The patient, a ten-year-old boy, had a negative family history. He was taken ill with tuberculosis of the ankle when two and one-half years of age. After four years of ailment, two years of which he spent in a hospital ward, the foot was amputated. There was prompt extension of the disease into the knee and thigh, the lower third of the femur being involved. He was sent home from the hospital where the amputation was performed, with three discharging sinuses. He was finally admitted to the Home for Crippled Children, in Newark, New Jersey, where tuberculin and bismuth paste treatment was begun in March, 1916. The brace which he had worn was discontinued, and a posterior plaster splint was applied instead. At this writing, one of the sinuses has completely healed, and the other two are about to close. The patient has greatly improved in every way, and it is only a question of a few months before he will be discharged cured. I base this prognosis particularly on the X-ray findings.

If it were within our ability to discern the predominant process in each case, we could apply these various therapeutic methods singly with success. However, the principal cause of the neglect of these methods was the failure to judge correctly the predominant condition present in every case. So that these various therapeutic agents were wrongly applied and, of course, were rapidly discarded. Why not apply them all in every case? Surely the vaccine will not interfere with the action of the bismuth paste; nor will tuberculin interfere with vaccine treatment; nor will immunization interfere with vaccine treatment; nor will immunization interfere with the proper use of orthopedic appliances. Each one of these therapeutic measures mentioned above—and which will be described in further detail later on—serves its own purpose and fortunately does not interfere with one another. Their combined use will lead to greater results which will not only help the victim, but also those who fall within the sphere of his influence. Then only shall we remove from the patient the consciousness of disease and open the wider field of employment to him. We shall remove from his mind the fear of transmission of the disease to posterity, and in a great many instances remove the barrier to matrimony. And lastly, but not least, is the fact that in the case of a patient cured by tuberculin, the orthopedist will be able to decide the exact time for the removal of the various appliances. This necessarily always had to be a matter of guess, as the orthopedist was never certain whether the joint is merely quiescent or cured, and therefore frequently insisted on prolonging the wearing of these appliances for a number of years, even though the patient seemed entirely well. With the danger of a relighting of the infection removed—the element of guess is eliminated—and both the patient and the orthopedist need not fear the removal of the appliances.

5. *Deformity.*—Orthopedic appliances are essential to limit functional destruction to a minimum, also to provide for the rest the part requires during the healing process.

The combined therapy is the only rational treatment for a combination of pathological processes.

General Hypersusceptibility

The degree of generable hypersusceptibility in bone and joint tuberculosis is exactly opposite to what it is in glandular tuberculosis; the closed variety having the greater degree of hypersusceptibility, and the open variety possessing the lesser amount of hypersusceptibility.

In the tuberculin treatment of bone and joint tuberculosis, we have two main varieties of processes to recognize. The closed variety, where the tubercular process is limited in or around the joint, the infection being purely tubercular in nature and therefore remains more or less circumscribed; and the open variety, where the destruction is considerable and where a mixed infection had led to an abscess formation which had broken open upon the surface of the body. The general hypersusceptibility holds the exact contrary position with regard to its degree in the open and closed as is true in the glandular tuberculosis. In bone and joint tuberculosis the greater degree of hypersusceptibility exists in the closed variety, whereas in the open type, the general hypersusceptibility lessens with the length of time that the disease has persisted. The highest degree of hypersusceptibility most often occurs in the earliest cases and it is particularly emphasized that where the diagnosis is doubtful and the tuberculin test is indicated, a severe reaction might be most detrimental. During the period of lessened tolerance after such a reaction (negative phase) an extension of the process is very apt to occur. In older cases, the tolerance increases through a long series of auto-inoculations and the degree of hypersusceptibility varies from a moderate amount to its absence altogether. In those cases where the tolerance is almost absent, the tubercular process has been overcome by a naturally acquired resistance. This represents the class of cases that responds readily to the injections of bismuth paste, without any other treatment.

Beginning Treatment.

It follows from the degrees of hypersusceptibility as described above that in early closed cases of tubercular joints, it is best to begin treatment with the fourth dilution

and in cases where the disease shows an acute condition, the fifth dilution is more strongly indicated. It is always necessary to bear in mind that the conversion of a closed case into an open one is always considered by the laity as a distinct retrogression in the condition and if it occurs during the tuberculin treatment, it might lead to a discontinuation of the treatment. Since a severe reaction will encourage the disintegration of tubercular tissues and since disintegrated tissues in a great many instances cannot be absorbed, it will lead to increased pain from pressure and finally to the breaking open on the surface with the formation of a sinus. It is therefore necessary to exercise a great deal more care in the treatment of closed conditions than in the treatment of open ones.

As a general rule 0.00001 c.c. of OT is not too large a beginning dose in the closed variety, except in recent acute cases, where 0.000001 c.c. of OT would be more advisable.

In the case of open bone and joint tuberculosis, we have by far an easier problem to deal with. We have channels for drainage; the disease, as a rule, is more effectively walled off from the surrounding tissues and any mishap during the tuberculin treatment will produce no serious results. We can, therefore, begin the treatment with the fourth dilution in cases where we suspect the hypersusceptibility to exist to a higher degree, as in very young children, or in cases of early infection. In long standing cases, it is quite safe to begin with the third dilution.

In the open bone and joint tuberculosis 0.00001 c.c of OT can always be the beginning dose, and in the older cases 0.0001 c.c. of OT is quite safe.

Conclusion of Treatment

In open joint and bone tuberculosis, after the conclusion of treatment with OT, it is sufficient to administer the usual course of BE as advised in the general plan (Chart III, page 60). Even if the sinuses and fistulas are still open, we can discontinue the administration of tuberculin after 0.20 c.c. of BE has been administered and continue the treatment of the case as described in the third section of this work. In the case of the closed bone and joint tuberculosis, it is advisable to conclude the tuberculin treatment as slowly as possible. The BE can

Conclusion of tuberculin treatment.

be administered by the slow method (Chart IV, page 60) and instead of doubling the dose of 0.10 c.c. pure BE, as a final test, we can continue the same increases beyond a 0.10 c.c. pure, until 0.30 or 0.40 c.c. pure BE is reached. The interval is always a week, and beyond the 0.10 c.c. dose ten days or two weeks may be the length of the intervals.

Results

The results obtained by the use of the *combined therapy* in bone and joint tuberculosis is so evident that it will require but a short trial to win over the most conservative opinion.

There is no class of patients that demonstrate the success or failure of a given therapy as definitely as those afflicted with bone and joint tuberculosis. This form of the disease is very chronic, and in a large number of cases produces permanent invalidism, in spite of the usual methods of treatment, so that when we speak of results obtained by the combined therapy as outlined here, there is no element of guess used as to the conclusions. When a month or two of treatment will begin to put color and flesh on an individual who has been pallid and emaciated for years;—when three or four months of treatment will remove pain and tenderness that have persisted for a long time;—when a year of treatment will close sinuses and fistulas that have been discharging for a decade or longer, and will remove the individual from the bed which he has occupied for the same length of time, and again place him among normal human beings,—there is no element of guess used when we pronounce this therapy as most successful.

The adoption of this method of treatment in institutions where bone and joint tuberculosis is treated will multiply the favorable results by many times.

No hospital ward has a more characteristic appearance than one where bone and joint tuberculosis patients are treated; and the features which render it so characteristic are the lack of interest on the part of the doctors and nurses, and the pained or resigned expression on the faces of the invalids. The whole work carried on in such a ward can be summed up by the one word "drudgery"—change of dressings from discharging sinuses, weight and pulley, feeding, and a change of soiled linens form a daily routine. It is remarkable how this aspect changes when immuno-therapy

is instituted in such a ward. There is no work that raises the enthusiasm of the physicians so much as the successful application of immuno-therapy. And once there is a rise in the interest on the part of the visiting physicians, it is immediately reflected in the attitude of the nurses toward these invalids.

In the Home for Crippled Children, in Newark, New Jersey, this change was most marked when in October, 1915, this form of therapy was instituted. The nurses now feel that their work has been raised from "drudgery" to a professional duty, and constantly speak of the results obtained as "miraculous." Doctor Sidney A. Twinch, through whose efforts this therapy has been instituted at the Home for Crippled Children in Newark, now rightly characterizes the former treatment of those cripples as "The do-nothing-treatment."

With the exercise of patience every ambulatory case of bone and joint tuberculosis is curable.

In the ambulatory treatment of these conditions, the results are no less brilliant. I cannot recall a single case in a period of seven years that has proved an out-and-out failure. There were a few, that for some unknown reason left in the midst of treatment; a few more left before the conclusion of treatment, considering themselves cured, and then had to return later for the treatment of recurrence. But altogether these exceptions are so few in number, and these few present such evident reason for the seeming failure which had no relation to the therapy applied, that we could pronounce the curability of bone and joint tuberculosis as complete.

It is true that any one of the processes going into the formation of tubercular bone disease may be most prominent in given cases,—rendering it possible for the appropriate therapy to produce a complete cure. In such instances the other processes were present in mild form, and spontaneously disappeared after the eradication of the predominant process.

We cannot, however, depend upon the application of a

It is best to utilize the *combined* therapy even in cases where it is possible to distinguish the predominant process.

single therapy for two reasons. In the first place, it is but rarely possible to discover the predominant process, and the choice of the therapy may be wrong in the majority of cases. In the second place, two or more processes play equally important rôles in the vast majority of cases, making it absolutely necessary for a combination of therapeutic measures to produce a cure. It therefore follows that with the *combined* therapy here outlined, maximum results can be obtained.

The following are a few characteristic histories and illustrations which will bring out the essential points in the treatment of bone and joint tuberculosis. These are cases where the tubercular process itself was the predominant factor in the condition. In Part III a full description will be found of cases illustrating more particularly the factors aside from the tubercular process, that form the whole complex pathology of bone and joint tuberculosis.

A perfect example of the value of the utilization of the immune response is illustrated in the following history.

This patient lived in the best of surroundings—a trained nurse was with him from the onset of his trouble—special climate, a sleeping porch, and every conceivable comfort were provided for him—he was under the best of medical care. In spite of it all, there was an unfavorable progress of the disease. He is a ten year old boy, has a negative family history, and was always well. In December, 1912, he sustained an injury to his knee, which was not thought to be serious, and he only occasionally complained of pain. Four months later the knee became swollen and was treated for effusion. The following month, in a consultation at Johns Hopkins Hospital, it was pronounced tubercular, although the X-ray failed to find any evidence of it. A plaster cast was applied. Three months later the wrist joint of the right hand was swollen and painful. The wrist was put into a cast. The wrist joint cleared up after fourteen months of immobilization. The condition of the knee which was not improving, was followed a year and a half later by involvement of the right hip joint. The process in this hip was very rapid and acute. When the author first saw the patient (through the courtesy of Doctor Sidney A. Twinch) the boy had been steadily confined to bed for ten months. The right hip and the right knee were extremely swollen, shiny and of a bluish hue. Both hip and knee were the seats of numerous fistulous openings. The patient was extremely emaciated. Two months after the institution of tuberculin treatment all sinuses were closed; the pain and suffering disappeared. At this time, a year and a half since the beginning of tuberculin treatment, he is in perfect health, weighing about forty per cent. more than he did when tuberculin treatment was begun.

A better example of an insufficient immune response cannot be presented, for nothing but the stimulation of this immune response with tuberculin would have availed in this case.

FIG. 26.—THE EFFECT OF THE REMOVAL OF A LOCAL LESION IN A CONSTITUTIONAL DISEASE.

Patient, a young man twenty years of age.

This is another illustration of the futility, to say the least, of an extensive operation for the removal of a local manifestation of a constitutional affection. After the amputation, there was prompt extension to the hip and shoulder, and although the tubercular condition was of many years' standing, it took but one year's treatment to combat the disease with final closing of all the sinuses. Thus this case proved that tuberculin was effective not only in limiting the process to a local condition, but in healing the local condition as well.

Chapter V

RENAL TUBERCULOSIS

The literature on the subject of renal tuberculosis is too meagre to serve as a basis for a fair estimation of the value of tuberculin in this condition.

Neither experience nor the literature on tuberculosis can be said to throw any light upon the subject of the treatment of renal tuberculosis by means of tuberculin. The immuno-therapist is never consulted in the early stages of the disease for two obvious reasons: The early symptoms bring the patient to the genito-urinary specialist or the gynecologist, if indeed a specialist is consulted at all; and again if the general practitioner is consulted, the diagnosis is rarely made until there has been a severe extension of the disease. The early diagnosis of renal tuberculosis is difficult in any case. When we consider that this disease falls in the province of the genito-urinary specialist or gynecologist, a systemic treatment like tuberculin or vaccine administrations would have to obtain spectacular results before it would be generally adopted. And just here the immuno-therapist can offer the least by way of advice either through his own experience or through the literature on the subject of tuberculin in tuberculosis.

In view of the bad prognosis in renal tuberculosis with the usual treatment, there can be no objection to a wider use of tuberculin.

A closer analysis of the subject of renal tuberculosis with reference to the source of infection and the complicity of the structure of the organs involved will no doubt bring home to the impartial reader the fact that tuberculin in genito-urinary tuberculosis is the most rational treatment. Then the few cases in my own experience that I can report together with the number of cases reported in the literature, will suffice to indicate that what in theory may be found rational, can be brought about in practice.

As to the source of infection: Tuberculosis of the genito-urinary tract is not a primary infection. The lesion first appears in the kidney and then travels down to the

bladder and so on. But, how does the tubercle bacillus find lodgment in the kidney in the first place? This question can have but one answer, and that is: Through the circulation. The kidneys form the main filters of the body. All products of digestion and assimilation, internal secretions and all else that forms in the body for the utilization of the body cells everywhere, must pass through the kidneys; and through a marvelous mechanism, the products necessary to the organism are allowed to pass on and the poisonous products, as well as the foreign material such as bacteria, are made to pass out of the system by way of the urine. Although it is difficult to find tubercle bacilli in the circulation, their presence there has been demonstrated. When these tubercle bacilli pass through the kidneys during a period of temporary insufficiency or of kidney irritation due to a temporary over-taxation caused by the passing through of an undue amount of irritating substances, tubercle bacilli may find lodgment there and start a lesion. The source of infection is usually somewhere in the lymphatic system, especially in the mesenteric glands. Mediastinal or mesenteric gland tuberculosis may exist in mild form undiscovered and offers the main source of infection for renal tuberculosis.

The source of infection in renal tuberculosis is outside of the urogenital apparatus.

In view of the existence of a distant source of infection, what are the chances for recovery through surgical interference alone? The removal of a kidney is an operation of considerable magnitude and serves to increase the hypersusceptibility to a high degree. The infection of the remaining kidney from the original source becomes even more likely than the infection of the first kidney, and we know with what frequency the infection of the remaining kidney occurs. Occasionally, the patient is cured after the removal of the kidney. The source of infection in that case completely healed, so that the removal of the kidney was sufficient to stop the rest of the tubercular process just as the radical operation in the glands in the neck does occasionally get beyond the area of infection. However, so numerous are

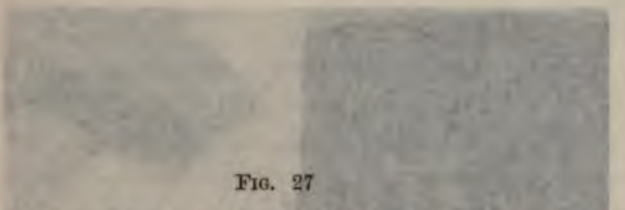

FIG. 27

Patient, a boy of twelve years. His father died of pulmonary tuberculosis. His mother and five other children are in good health.

He had whooping-cough at the age of four, scarlet fever and diphtheria at the age of six. Immediately after the scarlet fever pain developed in the left hip, and he had night cries. Six months later he began to limp and for three months was treated by five different physicians with liniments, anti-rheumatic medicines, etc., until finally one year after the scarlet fever he developed pain and swelling on the right ankle. He was brought to the Home for Crippled Children, in Newark, New Jersey, for treatment. Here a diagnosis of left tubercular coxitis and right ankle joint was made. The usual orthopedic appliances were applied, and his treatment was continued in the O. P. Department for one year. He was then admitted to the ward with the left hip involved and the right ankle discharging profusely. Buck's extension was applied to the hip and the ankle was dressed with dry dressings. During the year 1911, four sinuses developed on the right hip, discharging profusely. Two large cold abscesses formed on the hip during 1914. Several of the sinuses healed on the left ankle. At the time tuberculin treatment was begun, in October, 1915, the four sinuses on the hip and two on the ankle were still discharging profusely. Bismuth injections were given three times weekly. The patient was up on crutches by February 23, 1916. A photograph of the healed condition is shown in Fig. 29, which was taken in March, 1916.

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Fig. 27.

FIG. 28 IS AN X-RAY PHOTOGRAPH OF THE PATIENT SHOWN IN FIG. 27 AND SHOWS THE TOTAL DESTRUCTION OF THE HIP JOINT WITH SINUSES EXTENDING INTO IT.

FIG. 29 SHOWS THE SAME PATIENT AS IN FIGS. 27 AND 28 AND SHOWS A COMPLETE CURE.

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FIG. 30

Patient, a boy eight years old. Family history negative.

In May, 1914, pain and swelling developed in the right ankle, and in spite of wet dressings and an incision, which evacuated large quantities of pus, pain was incessant for fifteen weeks, the child screaming day and night most of the time. By this time the left hip became sensitive. Until August, 1915, he was treated in the O. P. Department of the Home for Crippled Children, in Newark, New Jersey. But his suffering became so intense that on that date he was admitted to the hospital ward. Buck's extension was applied to the left leg, and dry dressings to the right ankle, which was discharging a very offensive pus from four sinuses.

On October 14, 1915, tuberculin treatment (my method) was begun by Doctor Sidney A. Twinch, of Newark. On November 11, 1915, a fluctuation over the outer aspect of the thigh threatened to break and was incised by Doctor Twinch. Two weeks later bismuth paste injections were begun and administered twice weekly, both in the left hip and in the right ankle. After a few bismuth paste injections in the right ankle, the astragalus came away through one of the sinuses. All sinuses closed in December, 1915. One of them reopened two weeks later but finally closed again. There was an immediate response to tuberculin treatment, in this case the child improving in weight and strength, and requiring but a comparatively short bismuth paste treatment to close all the sinuses.

FIG. 30.

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FIG. 30.

FIG. 31.—SAME PATIENT AS FIG. 30.

This X-ray of the hip taken after bismuth injection shows the long sinuses. The stereopticon X-ray reveals the sinus going clear around the hip joint. It could be seen at a glance that any attempt at spontaneous healing would have rendered irregular healing and encysting of parts of the sinuses extremely liable, with consequent recurrence. This was prevented by bismuth paste injections.

FIG. 32

This patient, a boy nine years old, has a negative family history. When he was eight months old, the baby carriage in which he was sleeping fell down a flight of stone steps. After this his legs always seemed sensitive on handling, but he was given no treatment.

At one year of age he walked, and neither limped nor showed any signs of pain for six months. Then the left hip became painful. The tubercular nature of the condition, however, was not discovered until April, 1911, when he was brought to the Home for Crippled Children, Newark, New Jersey, after three years of ailment. A plaster spica was applied to the left hip, but the condition became so acute that in less than two weeks he was admitted to the hospital ward, with Buck's extension replacing the plaster spica. During the following few months abscesses with resulting sinuses developed all around the hip and thigh.

During the following year the abdomen began to grow very large, with the development of distinct signs of tubercular peritonitis. When the author first saw this patient in October, 1915, the boy had not left his bed in the hospital since April, 1911. Five or six fistulous openings around the hip and thigh oozed a thick creamy pus. The abdomen was greatly distended with the liver and spleen reaching down to the brim of the pelvis.

This case illustrates an extent of the tubercular process which was beyond the control of the surgeon, and what is more serious, it seemed beyond the reach of the patient's healing powers. The promptness with which this patient responded to the tuberculin treatment leaves no room for doubt as to the efficacy of tuberculin in tubercular affections. The X-ray photograph of this patient (Fig. 33) shows the extent of the tubercular process in the hip; and Fig. 34 shows the same patient cured, fifteen months after the beginning of tuberculin treatment.

FIG. 33.—X-RAY PHOTOGRAPH OF THE SAME PATIENT AS FIG. 32, SHOWING THE SINUSES FILLED WITH BISMUTH PASTE—NOTE THE ALMOST COMPLETE DESTRUCTION OF THE HIP JOINT.

FIG. 34.—SHOWS THE HEALED CONDITION OF THE SAME PATIENT AS FIG. 32 ALL THE SINUSES CLOSED, THE SPLEEN BARELY FELT BELOW THE MARGIN OF THE RIBS, THE LIVER ONLY TWO INCHES BELOW, THE ABDOMEN FLACCID,—THE BOY TO ALL APPEARANCES IN PERFECT HEALTH.

the cases where there is no benefit to the patient or where there is extension of the disease following the removal of the kidney, that the operation cannot be called a success.

As to the complicated mechanism of the organs involved: It is well known that the treatment of any part of the genito-urinary tract is very difficult and complicated, no matter what the cause of the pathological process may be. We all know how prone to chronicity is any condition arising in the kidney or in any other part of the genito-urinary tract. When a posterior urethritis remains for years, it is not because the infection with the gonococcus differs from the infection with any other organism, for, when the colon bacillus produces a pathological process in the pelvis of the kidney, it is equally tenacious. Even the non-infectious diseases attacking the kidney leave permanent damage behind. We need only recall nephritis complicating scarlet fever, or diseases causing an interstitial connective tissue change as in an interstitial nephritis, to realize how susceptible to damage the kidneys are. It is the complicated mechanism of the genito-urinary tract that renders it vulnerable, not the nature of the process attacking it. Hence, permanent damage depends less upon the virulence of the process than upon the length of time such process is allowed to go on without being checked.

The urogenital tract is so complicated and delicate that it is easily susceptible to permanent damage.

It therefore follows that in renal tuberculosis, the proper treatment must be instituted as early as possible and that many symptoms persisting beyond such treatment are due to the permanent damage done before treatment rather than to the persistence in spite of the treatment of the original pathological process.

The early treatment of renal tuberculosis naturally depends upon the early diagnosis of the condition. But just here the greatest difficulty arises. Early tubercular processes are usually circumscribed, very slow in progress, and thus exercise very little influence upon the function of the kidney. The patients at this time are usually in robust health

To obtain ideal results with tuberculin it must be applied before permanent damage has resulted.

and merely go to the family physician complaining of an annoyance, which usually consists of frequent micturation, especially at night. The possibility of a tubercular affection in the kidney is remote from the physician's mind. Every conceivable condition that might occur in the bladder, urethra or prostate is suspected, and the patient treated for it. If, for instance, the male patient gives a history of a gonorrheal urethritis, then, of course, the symptoms are easily explained on those grounds and the patient is subjected to all sorts of instrumentation and treatment. With the progress of the disease, the diagnosis of cystitis is made and is followed by irrigation of the bladder, prostatic massage (encouraging an active lesion in the prostate if a tubercular infection has reached it) and various other means directed against a supposed gonorrheal infection. When the process is still further advanced, the symptoms referable to the kidneys begin to be more pronounced; pus in the urine, perhaps blood in the urine, backache radiating toward the pelvis; all these symptoms bring the diagnosis of renal calculus, and in the female many pelvic disorders are suspected. Finally, the diagnosis of renal tuberculosis is made, sometimes by a careful study of the patient through expert assistance, sometimes by chance as in the case mentioned in connection with mixed infection (page 163), where the diagnosis of tuberculosis was made upon the discovery of tubercle bacilli in the thick pus, which took the place of urine. Occasionally, the X-ray finds an enlarged kidney without calculus and raises the suspicion of tuberculosis.

But just here we meet with the greatest difficulty, as an early diagnosis is rarely made.

To sum up, the diagnosis of renal tuberculosis always comes too late for the institution of early treatment principally for the reason that the usual methods for making a diagnosis are complicated and generally require a specialist. The result is that the general practitioner tries all available treatment for any other possible disease until he finds his treatment hopeless and refers the patients for expert advice. *The diagnosis of renal tuberculosis by means*

of tuberculin is by far the best at our disposal, for it is the only means for early diagnosis. With tuberculin, diagnosis can be resorted to by every physician and in every locality. The interpretation of the positive finding is simple in the case of renal tuberculosis and if the multiple method of tuberculin inoculation is practiced (see page 23), it is devoid of danger. Frequent micturation in an otherwise healthy individual should always be the subject of suspicion and a tuberculin test resorted to at once. If the case is not tubercular, the tuberculin will do no harm. If the case is tubercular, the harm done by a constitutional reaction, even if severe, can not be considered in comparison to the harm that comes to the patient from long delayed diagnosis and from instrumentation, bladder irrigation and other treatments that are resorted to, previous to the diagnosis, either for the treatment of supposed conditions, or for the diagnosis itself. It is quite true that were we to suspect a tubercular condition in every case where a definite diagnosis cannot be established, and where the patient complained of frequent micturation, the vast majority of patients will prove negative to the tuberculin test. I have never yet found a patient resenting the test when it proved negative and when it was explained that through the test we have excluded even the remotest possibility of an active tubercular affection. On the contrary, the patient is grateful to the physician for his endeavor to establish an early diagnosis of a suspected condition.

With the subcutaneous tuberculin test an early diagnosis is possible. It needs only to be properly applied and correctly interpreted.

With an early diagnosis established, how shall we proceed with the treatment? I do not know of any one who would advocate the removal of a kidney with an early lesion. There remains only the hygienic-dietetic-and-climatic treatment to be instituted for the patient when an early diagnosis is made. And what can that offer us? Unlike the patients with pulmonary tuberculosis, this class of patients are in fine physical condition, and if a fine physical condition did not prevent the lesion from

Once an *early* diagnosis is made, no other remedy can prove effective in limiting the process as well as eliminating the source of infection except tuberculin.

starting in the kidney, how can we expect treatment which depends upon the improvement of the physical condition, to cure or even check the disease? Here we deal with a combination of circumstances all of which are already favorable to the production of a natural immune response against the tubercle bacilli, except that the mechanism producing the immune response is faulty. The stimulation of this mechanism with tuberculin remains the only logical early treatment. All other resources necessary for the patient's own defense are present in sufficient quality and quantity.

By the time a diagnosis is made under ordinary methods, permanent damage has already resulted.

When once a diagnosis is possible without tuberculin, the patient presents a picture of chronic inflammation that no other chronic condition presents. Especially is this true in the male patient. He is never free from pain and discomfort, cannot have a peaceful night's sleep on account of the necessity of frequent urination, often cannot do without a permanent urinal, because of incontinence; cannot take a ride in any vehicle because the jars cause agonizing pains; in short, the advanced renal case is subject to every conceivable discomfort that makes life unbearable. Most of these symptoms come from the extension of the disease into the bladder, the prostate and the urethra. A great many small ulcerations which have been produced traumatically by instrumentation form the seat for new tubercular infection. Although no one but the skilled specialist should resort to cystoscopy and ureteral catheterization, they are nevertheless far too frequently resorted to. Many of these instrumental examinations are made in spite of the knowledge that they could in no way improve the condition of the patient, but which, on the contrary, may aggravate the condition temporarily or even permanently.

In the exclusive interest of the patient, what would seem to offer the best procedure in the treatment of renal tuberculosis in the state in which it is discovered in the majority of instances? It is quite true that a removal of a kidney has occasionally cured a case of renal tuberculosis,

even with ulcerations of the bladder. I am quite certain that in these instances a closer analysis would reveal that the principal cause of the patient's condition at the time of operation lay elsewhere than in the tubercular infection. For example: In a case of renal tuberculosis where the tubercular infection is more or less spent, but where the ulcerations in the bladder and the predominating pathological processes in the kidney are due to mixed infection, the kidney will act as a foreign body. The stroma is entirely destroyed by multiple abscesses so that the removal of the kidney is sufficient to cure the patient. Again in a case of calculus with accompanying hematuria or pyelitis producing the predominant symptoms but where a small quiescent tubercular lesion exists, the removal of such a kidney will result in a complete cure. This is analogous to the condition that exists in bone and joint disease where the tubercular infection has healed and the sinuses are kept open by mixed infection or irritating accumulations, the removal of which by bismuth paste is sufficient to complete the cure.

The removal of the kidney is in most instances an attempt to remove a local lesion in a constitutional disease.

On the other hand, in the majority of cases where the principal cause of all the symptoms is a slowly progressive tubercular infection, how can we expect to cure the patient with the extirpation of one kidney? Not only do we leave behind a tubercular process in the urinary tract below the removed kidney, but with the added burden suddenly thrown upon the remaining kidney, its resistance may be momentarily lowered and it may become infected from the original focus. The hypersusceptibility being increased as a result of the operation, will more than encourage this occurrence and bring about a most hopeless condition.

General Hypersusceptibility

The general hypersusceptibility in renal tuberculosis is on a par with the general hypersusceptibility in closed glands so long as the infection is limited to the lesion in the kidney.

The general hypersusceptibility in early renal tuberculosis is of a low degree.

That is, it is not of a very high degree and would require about 0.10 c.c. of the second dilution to cause a reaction. There are, of course, a great many exceptions, such as the hypersusceptibility in early cases of renal tuberculosis following an infectious disease or in cases where the focus of the infection is active, in which instance we would consider the hypersusceptibility due to that focus and not to the lesion in the kidney.

The general hypersusceptibility in advanced cases is of two distinct grades: It is high where there is an active ulcerative process in the kidney and bladder. It is low in cheesy or fibrous kidneys, where the process is continued by mixed infection and not by tubercle bacilli.

In later cases, there are two distinct grades of hypersusceptibility. On the one hand there is the class of cases with extensive ulcerations of the kidney, with complicated bladder ulcerations. In these cases the lesion is active, the susceptibility is extremely high and occasionally will require a sixth dilution for the beginning of treatment in order to avoid reaction. On the other hand, we have renal tuberculosis consisting of calicies, which are converted into sacks of cheesy material or cold abscesses. Here the entire kidney acts as a foreign body, its function being entirely destroyed. It is apt to have very little active tubercular inflammation in it. The tubercle bacilli that are still found in the urine are of a fungoid character, while the ulceration in the bladder and elsewhere is continued merely by the presence of the acid urine and mixed infections. In such a condition, the patient is apt to be in good physical condition with very little loss of weight, in spite of the ever-present extreme discomforts. The susceptibility in these cases is very low and occasionally does not exist at all. The latter is the condition in which the removal of the kidney without any other treatment very frequently cures the patient.

The presence of hypersusceptibility in various degrees and its absence altogether in renal tuberculosis may be of service to the surgeon in determining upon a nephrectomy. For instance, if with a tuberculin test a considerable degree of hypersusceptibility is discovered, before a contemplated operation, it may serve as a warning against it and a course of tuberculin inoculations should be given instead, or pre-

paratory to the operation. On the other hand, if the hypersusceptibility does not exist at all, or only to a very mild degree, it is sufficient evidence that the tubercular infection has subsided and that the condition in the kidney and elsewhere is merely the result of the tubercular infection. Then surgical interference can be instituted with a fair degree of safety, and a reasonable amount of success may be expected.

The tuberculin test as a guide to surgical interference.

Beginning Treatment

In early cases of renal tuberculosis, it is quite safe to begin treatment with the fourth dilution, and when it required the second dilution to cause a reaction during a test, it is safe to begin the treatment with the third dilution. In more advanced cases our judgment as to the amount of tuberculin in the beginning of treatment must be influenced by the nature of the symptoms at hand. Thus, if the patient runs an abnormal temperature, for which no other cause can be found than the tubercular process, the fifth dilution is indicated for the beginning of the treatment. That is also true in a case of persistent hemorrhage. However, if the severer symptoms are caused by other conditions than the tubercular process—conditions such as calculus, mixed infection, pyelitis, etc.—tuberculin treatment can be instituted with the fourth dilution. It is, however, better to treat the mixed infection until the temperature is normal (see page 175) before tuberculin treatment is commenced.

The beginning treatment with tuberculin should wait until an acute mixed infection is controlled.

Conclusion of Treatment

The conclusion of treatment as far as tuberculin is concerned is more like that in a case of pulmonary tuberculosis with cavity formation than in a purely glandular type. It is best—as is advised in the third section of this work—to spread the conclusion over as long a period as it takes to treat the patient for the complications. Once the B.E. is reached, the increase of the dose can be made regularly

In most cases the conclusion of treatment is best accomplished by the slow BE method.

by 0.05 c.c. and continued until 0.30 c.c. or even 0.040 c.c of pure B.E. is reached. It will thus take 25 to 30 inoculations given at weekly intervals while administering the B.E.1. and ten-day to two-weekly intervals when administering the pure B.E. This will carry the conclusion of treatment over a period of a year, allowing ample time for any other treatment that may be necessary. It is especially advisable to continue the treatment during the convalescence from a nephrectomy and for some time after. Of course, if a nephrectomy can be postponed until after all the B.E. inoculations have been given, it would be to the advantage of the patient; but, if the condition of the kidney is such as to require the operation at the earliest possible moment, it may be performed after the conclusion of the OT administration.

In tuberculin diagnosed cases, the conclusion is simple.

In incipient cases of renal tuberculosis, such as are discovered through the tuberculin test, the conclusion of treatment is very simple. The process is limited to a small, usually circumscribed, area in the kidney, and is not unlike the process in closed glands. After the usual conclusion with OT the short course of BE is administered, followed for two years by the tri-monthly test.

Chapter VI

PULMONARY TUBERCULOSIS

Tuberculin has been more widely used in pulmonary tuberculosis than in any other form of the disease.

I have no doubt conveyed the idea that most phases of tuberculosis have been neglected from the standpoint of immuno-therapy. This statement, however, does not by any means apply to pulmonary tuberculosis. This form of tuberculosis, I must admit, has been given its share of scientific labor. I need but refer the reader to the exhaustive literature on the subject and he could spend the remainder of his natural life perusing it.

The literature on this subject, however, bears out the fact that tuberculin has been applied mainly as a last resort measure.

Tuberculin has been used in pulmonary tuberculosis more extensively than in any other form of tuberculosis and the results of its use have been published in nearly every country. However, one cannot help but gain the impression from reading these reports that tuberculin has been applied as a last resort measure, and that the incipient case has been considered easy of cure either through climate, sanatorium treatment, or rest and hyperalimentation; in short, the hygienic-dietetic-and-climatic treatment is alone in consideration and tuberculin is used only when this method produces no results.

In Germany, however, the value of tuberculin in early cases of pulmonary tuberculosis has been recognized and its increased use there, in the last decade, has evinced a marked diminution in the death rate from pulmonary tuberculosis. So marked has this reduction in the death rate been, that the public demand for sanatoriums where tuberculin is administered has become quite general; and as a result, ninety per cent. of all institutions in Germany where pulmonary tuberculosis is being treated are now using tuberculin together with the hygienic-dietetic measures.

The actual origin of the public education in Germany regarding the use of tuberculin is the accurate statistics kept

The lack of proper statistics has prevented a public demand for tuberculin.

by the German Government. In this country statistical reports of disease and the causes of death are in such a deplorable state that the public is not in a position to compare the results obtained by the use of tuberculin in one community with the results obtained without its use in another community. It is, therefore, useless for the medical profession in this country to await the public demand for tuberculin. On the contrary, it remains for the general practitioner to wake up to the truth as shown by the records supplied by Germany, and help educate the public to its advantages.

The human race possesses a natural immunity against tuberculosis.

Through innumerable autopsies in every part of the world, on subjects having died from other diseases than tuberculosis, and through thousands of autopsies made upon subjects having died through accident in apparently perfect health, it has been established that tuberculosis is a universal disease. In fact, from most conservative sources, we gather that hardly twenty per cent. of the human race escape a lesion in the lung, and yet the percentage of deaths due to pulmonary tuberculosis is hardly one-tenth of that number. Thus, a fact which must remain undisputed is brought home to every one of us; that the human race possesses a natural immunity against tuberculosis.

Those who succumb to the disease lack sufficient immune response when first infected.

The sole cause, then, for the morbidity of the disease is the falling short of the amount of natural immunity necessary to check it. It is a very small minority of cases that possess no immunity or so very little that they succumb to the hasty form of tuberculosis. In fact, we can, with certainty, deduce that the mechanism of active immunization plays a rôle in nearly every case of pulmonary tuberculosis in its incipiency—acting for a longer or for a shorter time as the case may be—and finally wearing itself out until the disease spreads and causes death. Very little stimulation of the protective mechanism would have been required to turn the balance in favor of these victims.

Immuno-therapy alone could have supplied this stimu-

lation and it remains clear that such a stimulation if supplied early, would prove more effective and would leave less permanent damage in the lungs than if applied late in the disease. The question, however, that would arise is: How are we to judge, in early cases, those that possess the necessary amount of natural immunity and those that fall short of it? Would we not be apt to treat a great many cases with tuberculin that might have gotten well without it? These questions can be very easily answered if we recall how large is the number of cases of incipient pulmonary tuberculosis that come quite early in the disease, and in spite of the best in the way of hygienic-dietetic-and-climatic treatment, progress unfavorably. The careful treatment with tuberculin would do no harm to those who would have gotten well without it; on the contrary, it would fortify them against a recurrence, and at the same time would be the means of saving the lives of many who had insufficient immune response to begin with. By way of illustration, I shall mention one recent report. It came from the Loomis Sanitarium and was made by Doctor H. M. King. The report showed that in spite of sanitarium treatment under the best posible conditions, over twenty-nine per cent. of the incipient cases treated at that sanitarium died of a recurrence of their disease within ten years after discharge. Many such reports can be found throughout the literature; very few, however, could show even such favorable results. In contrast, if we examine into the results of immunotherapy in incipient cases of tuberculosis reported, we shall find that the percentage of permanent cures runs close to one hundred per cent., and this from unquestionable authority. The difference can easily be explained: the hygienic-dietetic measure is one that aims to strengthen the individual as a whole with the hope that it will also increase his natural defense against [illegible]. In a large number of incipient cases [illegible] per cent.—it succeeds. By even [illegible]

An artificial stimulation of the immune response is by far the most rational treatment, and the earlier in the disease it is applied the surer the response, and the less permanent damage results.

bility remains; and, while in the thirty per cent. of fatal cases it was the means of an early recurrence and death, in the favorable cases it still remains a menace—even beyond ten years.

The artificial stimulation of the immune response cannot interfere with the natural immune response. That is beyond question. Where, then, is the objection to the use of tuberculin in such cases that would have gotten well on the hygienic-dietetic treatment alone? The only danger lies in the too frequent and in the severe reactions caused by a faulty technique. The fault, therefore, is not in the tuberculin itself, but in its method of use, and once we have established a method of administration which avoids severe and frequent reactions, the objection to tuberculin, per se, can no longer be advanced as a justification for its neglect.

The artificial stimulation of the immune response does not interfere with the natural immune response.

Contra-indications

There are no real contra-indications to the use of tuberculin.

From the outset I want to be understood as denying the existence of contra-indications. I do not believe that real, genuine contra-indications to the use of tuberculin exist. The harmful results recorded were not obtained by the use of tuberculin under the wrong conditions, but from the wrong method of use of tuberculin; and the failure to recognize this fact has produced a long list of "contra-indications." Were we to take a census of the conditions put forth by different investigators as "contra-indications" to the use of tuberculin and take them all seriously, there would be very few cases left for tuberculin therapy. For instance:

Fever may be a temporary contra-indication when caused by mixed infection.

FEVER is maintained to be a most constant contra-indication in spite of the fact that it is very frequently a symptom of incipient tuberculosis where tuberculin has its most effective field. However, as mentioned above, fever may be produced by mixed infection. The failure to differentiate between this fever and that produced by the tubercular infection has occasionally led to an improper application of the tuberculin treatment, producing harmful results in cases of

fever. There is no antipyretic as effectual as tuberculin in *tubercular fever.* The fever produced by mixed infection should not exclude the use of tuberculin altogether; it should postpone its use until the mixed infection has been cleared to the extent of reducing the temperature. However, if the mixed infection resists all treatment, and the fever which it causes continues the wasting of the patient, tuberculin will have no effect.

DEBILITY. Debility is another "contra-indication" very frequently mentioned. As stated above, the loss of reactive properties on the part of the patient forms a *natural* limitation and not a contra-indication to the use of tuberculin. It is true that the use of tuberculin in cases suffering from debility will produce absolutely no results, but neither will it cause any harm. And since we cannot determine absolutely, until the tuberculin has been tried, whether or not the reactive properties of an individual are lost, the use of tuberculin will occasionally meet with a response where the symptoms of debility were pronounced. Thus, by excluding tuberculin from a whole class of cases, we might omit the use of tuberculin where it would prove of inestimable value.

Debility is a natural limitation not a contra-indication.

True, the number of such cases is very small, but it is also true that trying tuberculin for a short time in cases where the immune response has been exhausted will produce no harm, as a reaction cannot occur. In the practice of medicine, it is axiomatic that the use of a remedy is justifiable in many cases where it produces no beneficial results, but proves harmless—so long as that remedy is efficient in the salvation of the few.

The use of tuberculin is justifiable in cases of debility as it can produce no harm.

That tuberculin might awaken an immune response is particularly true in those cases of cachectic tuberculosis with only small areas of lung involvement. We know that the effect of tuberculin on the blood is distinctly stimulating, both the red and the white blood cells increase far more rapidly than through any other form of treatment.

Tuberculin may awaken a response in a few cases where the immune response was thought to be absent

Classification

1. Incipient.
2. Chronic or Slowly Progressive:
(a) fibrous phthisis;
(b) calcareous and ulcerative.
3. Acute or Active:
(a) febrile;
(1) mixed infection,
(2) auto-inoculation;
(b) afebrile;
(c) hemorrhagic;
(1) traumatic,
(2) ulcerative.

The classification of pulmonary tuberculosis is by no means an easy matter and it is not surprising that almost as many varieties of classifications exist as there are writers on the subject. The structure of the lung tissue, the variety in the pathological process, to which added the great difference in individual susceptibility and resistance to the tubercle bacilli, all taken together tend to make for not only a variety in the gross pathological difference, but also in the symptoms which they bring about. Fortunately, the task is not quite so difficult for the immunizator. In dealing with the immune response, we need take cognizance of the pathological difference in the lungs of different individuals only in as far as they produce a difference in symptoms and that only in a general way. As far as tuberculin therapy is concerned, only such differences can have any bearing upon it, as the presence or absence of hemorrhage, or the chronicity or the rapidity of the process involved. This classification therefore will depend entirely upon its reference to tuberculin therapy and if it differs materially from the usual classifications bearing on the stages of the disease, etc., it will find its justification in the fact that this classification is merely made to add to the simplicity of the tuberculin therapy. Accordingly, the tubercular processes in the lung are divided into the following three groups:

1. THE INCIPIENT PULMONARY TUBERCULOSIS. Under this group only such cases are considered which require a test to establish a diagnosis and which show physical signs before the presence of tubercle bacilli in the sputum.

2. THE CHRONIC OR SLOWLY PROGRESSIVE PULMONARY TUBERCULOSIS. Under this group are included the type of cases which persist for a long time, the natural resistance being sufficient to prevent an acute attack, but not quite sufficient to arrest the process; also those cases in which the process has been arrested one or more times with the light-

ing up of the infection under a change of conditions whether extrinsic or intrinsic. All patients with tubercle bacilli in the sputum are here included, embracing all cases, from localized infiltrations in the lung to those that have progressed for several years, and are now suffering from ulceration and cavity formation or calcification. For the purpose of greater simplicity, this group is subdivided into two types.

(a) Those with extensive infiltration, connective tissue change or fibrous phthisis.

(b) Those with calcification process, the calcarious deposit finally causing ulcerations and cavity formation. We shall not discuss here whether the action of the calcarious deposit as a foreign body is brought about by mixed infection or by the tubercular process, as this question has no bearing upon tuberculin therapy. But the decision as to whether there is a fibrous phthisis or cavity formation will have a great bearing upon the conclusion of treatment as will be indicated further.

3. ACUTE OR ACTIVE PULMONARY TUBERCULOSIS. Here we shall include the more active form of tuberculosis, the kind that progresses rapidly either through lack of the immune response or through an over stimulation of the mechanism of immunity by auto-inoculation, or through a rapid loss of strength, due to an excessive [illegible] of blood. In this group belong the greater number of patients who are considered as disqualified for tuberculin therapy, and at the same time stand particularly in need of something more than the present day treatment [illegible] favor. By a closer analysis we are [illegible] a considerable number of [illegible] be rescued with tuberculin. With a [illegible] harm that might be caused by [illegible] infrequent that the good to [illegible] saving the victims of the disease [illegible] possible harm. [illegible] and pyrexia are [illegible]

trolled tubercular process as by a mixed infection, and if we were to take fever as a general contra-indication we would lose a large number of cases that come under this class. A subdivision of this class into *febrile, afebrile* and *hemorrhagic* cases, enables us to further simplify treatment. For example, in taking up the first of these three, we must endeavor to analyze the cause of the fever and determine whether it is due to autoinoculation or to mixed infection. In the active afebrile group where the rapidity of the process is causing ulceration, the sole cause may be an insufficient immune response. Under the hemorrhagic group, we must take into consideration whether the hemorrhage is due to ulceration in the vicinity of larger blood vessels or whether the hemorrhage is traumatic, brought about by too great exertion when coughing, or by excessive exercise.

GENERAL HYPERSUSCEPTIBILITY. In pulmonary tuberculosis, as a rule, the general hypersusceptibility is much higher than in other forms of the disease. If we are to accept the theory that tuberculosis of the lung is the tertiary form of the disease and that the focus of the infection is in the glands or bones, whether in the immediate neighborhood or at a distance,—the hypersusceptibility must be high to begin with in order to allow of such extension into the lungs from a quiescent lesion. Again, lung tissue with the blood current running through it in such a perfect network invites auto-inoculation far more easily than does any other tissue. This auto-inoculation increases very materially the hypersusceptibility; so that here again we have a physiological paradox as in the case of the mechanism of immunity. The richness in the circulation tends to quickly overcome the tubercular infection when it localizes in the lung, but that very element causes too large a supply of antibodies and too ready an absorption of the poisonous proteins which cause the constitutional reaction, allowing at the same time an extension of the process. Thus the hypersusceptibility in acute pulmonary tuberculosis is very high.

The structure of pulmonary tissue, with its rich blood supply encourages autoinoculation which increases the hypersusceptibility.

In the presence of a tubercular lesion in the lung, the hypersusceptibility which accompanies all other tubercular lesions must be considered with reference to the lung lesion. Thus, it may happen that a large beginning dose of tuberculin may produce disastrous results in an old case of joint tuberculosis with fistulas, where the susceptibility would be low, but where the contrary is true because of an overlooked incipient apical tuberculosis. The third dilution would be safe in the case of joint tuberculosis without the lung lesion, but in the presence of the lung lesion the susceptibility is much higher, requiring a fifth dilution for the beginning treatment. In the case of multiple lesions, we must treat the patient with reference to the lesion which is accompanied by the highest degree of hypersusceptibility.

Treatment

INCIPIENT. As stated above, under the class of incipient cases of pulmonary tuberculosis we include only those with lesions in the lung which are difficult to detect, requiring, in a great many instances, the tuberculin test to establish a diagnosis. As soon as symptoms arise which define the diagnosis, as tubercle bacilli in the sputum or a hemorrhage, we no longer consider the case incipient. It therefore follows that the full amount of susceptibility in the cases coming under this class has not yet developed. They usually come to a physician complaining of a "hanging on" cough following a "bad cold," or an acute infection such as influenza, pneumonia, pleurisy, etc. Or, they come complaining of loss of weight, night sweat, lassitude, a general feeling of fatigue, or a general "run-down" condition, which persists for a while in spite of tonic treatment, good food, etc., until eventually a closer examination reveals a few râles at one or both apexes with perhaps a little dullness or increased fremitus. All these signs lead to a tuberculin test to establish the presence of an active tubercular lesion. The active pathological process has been brought

Hypersusceptibility is not so high in those cases classed here as incipient.

about by the presence of a small amount of hypersusceptibility left over from a previous tubercular process. Whether the previous process existed at the same time and was arrested or whether it existed as an adenitis in infancy or childhood, has no bearing upon the present condition. Any pathological process, however mild, forms a temporary traumatic area in the lung and acts as trauma in the etiology of bone lesions by attracting the tubercle bacilli and starting a tubercular process. The area of infection being small, the number of tubercle bacilli that come into play is as yet limited and as a result the protein poisons have not yet been set free in the circulation in sufficient quantities to increase materially the hypersusceptibility.

Beginning Treatment. The tuberculin treatment of incipient pulmonary tuberculosis is very simple. We can begin with the fourth dilution in a great many cases, especially in those cases where more than one test had to be made and where the amount of hypersusceptibility was thus more or less determined. If a fourth or fifth test was required (see page 23) before a constitutional reaction was produced. it is absolutely safe to begin the treatment with the third dilution.

Begin treatment in incipient cases with the fourth dilution, except in cases where a diagnostic test has shown that it may be safe to begin with the third dilution.

Conclusion of Treatment. In the incipient pulmonary tuberculosis, it is rarely necessary to deviate from the usual form of conclusion of treatment as outlined in the "Scheme of Dosage," for in limiting the incipient cases to those conditions where the tubercle bacilli are not yet present in the sputum, we have no more difficulty in its treatment than in a simple case of tubercular adenitis. After the conclusion of the series of inoculations with the first dilution of BE, there remains nothing further for us to do for the patient except the periodic tests over a period of two years for the possible return of hypersusceptibility.

The conclusion of treatment is very simple.

CHRONIC OR SLOWLY PROGRESSIVE. Among the slowly progressive cases of pulmonary tuberculosis we recognize by far the majority of patients that seek ambulatory treatment.

A great many of these patients have received more or less of the hygienic dietetic and climatic treatment, have been benefited by it but are now suffering from recurrences; many have gotten disgusted with this treatment because of the slow progress they were making toward recovery, have grown impatient at the length of time they were kept from their families, their occupations or their favorite haunts and have finally returned to their usual mode of living, taking any risks for the sake of being comfortable while they last. Others return to their homes and occupations from a sanatorium or mountain resort after slight improvement, either under the impression that they are cured, or in spite of the advice of the most expert in the profession. The amount of benefit thus gained wears off and they are soon found again in the doctor's office, denying emphatically that they are ill enough to go back to the sanatorium, and demanding ambulatory treatment so that they may continue their occupation. Particulary is this true among active and ambitious individuals to whom inaction is worse than tuberculosis. The enforcement of inaction sometimes hastens the disease in spite of the best treatment and climate. Just such patients will give the most gratifying results with tuberculin treatment. The usual optimism in the curability of their condition, added to the beneficial constitutional effect brought about by being kept at their occupation, go to make a most favorable prognosis for tuberculin treatment. In this group we have cases that cannot stand high altitudes either on account of the heart condition or on account of the existence of a chronic bronchitis, which in many instances makes sleeping in the open during cold weather impossible.

The great majority of ambulatory patients with pulmonary tuberculosis belong to the group of chronic or slowly progressive.

Tuberculin is the only treatment to which many of these patients will submit.

In every sanatorium are to be found a number of chronic cases with the tubercular condition progressing favorably. The most we can hope for in this class of cases is an arrest of the process. Patients with arrested lesions are returned home, the patient glad to get home and the

Tuberculin added to sanatorium treatment would increase the quality and permanency of the results obtained.

sanatorium congratulating itself upon obtaining such results. At the same time, it is an ever-present fact that of the arrested chronic cases that go back to their previous occupations, nearly all recur. Would it not be at least reasonable to have added tuberculin properly administered to the treatment of these patients and thus have gained a large degree of immunity against recurrence? Surely the tuberculin would not have interfered with any other treatment at the sanatorium. No one who has used tuberculin extensively will now assert that any case which progressed favorably through a number of years under the hygienic-dietetic and climatic treatment would have terminated otherwise than favorably if tuberculin had been added to the other treatment.

Again, we have the patients in whom the process slowly progressed through a number of years. During this time new areas of infiltration constantly occur during a period of lowered resistance, due to whatever cause, followed by connective tissue change during a period of heightened resistance. This see-saw process goes on for years, the advance in the disease never going far enough to kill the patient and the healing process never going far enough to cure the patient, until the time comes when the patient slowly dies of insufficient lung tissue for oxygenation. During any one of these periods of heightened resistance, an artificial boost would be sufficient to accomplish a cure. On the other hand, any preventive measure which would tend to avoid a period of depression would allow the healing process to continue long enough and accomplish the same purpose.

The relief produced by tuberculin in chronic ulcerative pulmonary tuberculosis calls for its use even in hopeless cases.

Again, we have a class of cases where the tubercular process has gone on to cavity formation with sclerotic changes throughout the lungs, dyspnea, cough and an unlimited amount of expectoration are the principal symptoms which are constantly present day and night. This process may go on for years before the patient is carried off. In the meantime he is in discomfort and a menace to

his surroundings. For in these cases, the number of tubercle bacilli present in the sputum is more abundant than in any other form of the disease. The cavity is filled with the best possible culture media for the tubercle bacilli and the lung forms the best incubator for their growth. These classes of cases are hopeless to begin with and therefore an extensive therapy like tuberculin therapy would seem a waste of time. But that is not the case. Just these cases seem to cry for "relief," and as they will often put it, "or death." A constitutional reaction in these cases will not very frequently occur, in fact, if it does occur, the effect is not at all alarming. At the same time, the relief which tuberculin will bring to the patient is so marked, especially when augmented by mixed infection vaccines, that it is almost criminal to withhold it. The cough may not be diminished by tuberculin, but its racking will be greatly lessened. The tight feeling in the chest which the patients describe as "a grip which seems to squeeze the breath out of their lungs" will be relieved to a varying extent. It is surprising in how many cases of this kind, the tubercle bacilli will disappear from the sputum, a fact which speaks loudest for tuberculin therapy even in hopeless cases. So that even if we are to ignore comforts to a hopeless case during the last months of his life, surely we must remember that we must prevent him from being a menace to his community.

Tuberculin will frequently remove the tubercle bacilli from the sputum.

Beginning Treatment. Although the chronic cases, whether they have the fibrous or the ulcerative form of the disease, possess a more or less controlled hypersusceptibility, it is best to begin with the fifth dilution of OT and continue in the usual way three or four weeks. If a distinct focal reaction is elicited by every inoculation, especially if accompanied by a local reaction—even if only mild—it is best to continue the treatment throughout, according to the scheme outlined in Table I, page 57. On the other hand, if the tuberculin seems to produce no impression on the patient's condition, better results can be obtained by a

In the beginning treatment a more rapid approach to the maximum tolerance may be advisable in a great many cases.

quicker approach to the maximum tolerance. This can be done by increasing the increase at every inoculation, instead of increasing the increase at every other inoculation, until a distinct focal reaction has been elicited by two or three successive inoculations. At this point, it would be best to discontinue the more rapid increase and return to the usual method of increasing the increase at every other inoculation, without waiting for a constitutional reaction. Should a constitutional reaction take place before we have reduced the rapidity of the increase, the usual indications following the constitutional reaction should be complied with; *i. e.,* after an interval of one week, resume the inoculations with a dose equivalent to the third last, and not only should the increase be reduced to the amount of increase given at the commencement of treatment, but this increase should not be increased more rapidly than at every other inoculation. (Table II, page 59.) From this point, the usual routine of doses is continued.

Conclusion of Treatment. The conclusion of treatment in a case of fibrous phthisis does not differ greatly from that required in a case of surgical tuberculosis. In a great many cases the removal of hypersusceptibility with OT would be sufficient to effect a cure as far as the tubercular infection is concerned. The localized hyperemia brought about by the focal reaction in response to the tuberculin inoculation is sufficient to encourage the already present tendency to scar tissue formation. Since a complete cure in fibrous phthisis is prevented by the tubercular process keeping slightly ahead of the scar tissue formation or healing process, the slightest delay in the progress of the infection plus the stimulation of the healing process by the focal reaction, makes a cure in this class of cases almost certain. However, since we very often encounter large areas of fibrosis in which the circulation is necessarily poor, it would be best to add a course of BE inoculations according to the principle laid down in Table III, page 60.

Treatment for the mixed infection may be most important in the conclusion of treatment.

The essential elements in the conclusion of treatment are the treatment of mixed infection, and the removal of the elements which first encouraged the spread of the tubercular process, as may be gathered from a complete physical examination and a more detailed history. I am referring to the possible presence of nasal obstruction, throat complications, chronic bronchitis, and anemia,—especially when due to constipation.

The supervision of the patient's mode of life and habits must continue during the two years that he remains under observation.

The habits of the patient must be regulated with a view to the normal existence which he is to resume from now on. We must take great pains to remind the patient that although he is no longer ill, he must not resume injurious habits which may have facilitated his infection in the first place. These instructions are more easily carried out by our rule of keeping the patient within our professional sphere for two years following the conclusion of his treatment. In these cases especially, the testing of the patient every three months should not be overlooked.

The conclusion of treatment in the ulcerative form of chronic phthisis should be carried out with the utmost care.

The greatest care must be exercised in the conclusion of treatment of the *ulcerative* form of chronic pulmonary tuberculosis. Here we have a condition similar to tuberculosis of the bone. Just as in bone tuberculosis a cavity may persist after the tubercular infection is ended,—so also in the ulcerated form of pulmonary tuberculosis with cavity formation, we must not expect obliteration of the cavity with the eradication of the tubercular infection by means of the tuberculin. Although there is a similarity in the process of formation of a bone cavity and of a lung cavity, we have an added disadvantage in the treatment of the latter, in as much as in a lung cavity we cannot by means of bismuth paste prevent the accumulation of suppurative material. In addition to that, we are constantly forcing infectious organisms into such a cavity by the process of inhalation. Fortunately, two factors exist which rescue this situation from becoming hopeless: the reflex cough, and perfect drainage by means of the bronchial tube. We must utilize these two factors

Opiates should be used very guardedly in cases of cavitation, as our only means of emptying the cavities is through the reflex cough.

to the best advantage so long as the cavity exists. And even though exhaustion and lack of sleep may make it necessary to employ remedies to lessen the amount of the cough, we must use them guardedly. By the too generous use of these drugs, infected and irritating material may become pent up which not only does harm by remaining in the cavity, but which, through further accumulation might be forced into the bronchioles and vesicles of the surrounding lung tissue, spread the infection, and even tend to produce a pneumonic process. It is self-evident, therefore, that we must keep our patient constantly fortified against mixed infection. A detailed description of mixed infection treatment and prevention, and methods that we must utilize to encourage the contraction of the lung cavity will be found in Part III of this work. I call attention to it here, in order to emphasize its importance. Tuberculin is hopeless here without attention to these details. Since the time necessary for the healing of a lung cavity is considerably longer than the healing of the fibrous form of lung infection, and as it is advisable to keep the patients under the influence of tuberculin while they are still under treatment, it is best to utilize the longer of the two methods of BE administration (Table IV. page 60.)

Treatment of the mixed infection should not be overlooked.

ACUTE OR ACTIVE. Acute pulmonary tuberculosis includes in its category the most difficult cases to be treated by any method, especially with tuberculin. At the same time, this class of cases count the greatest mortality among them, so that a special method of therapy becomes much more urgent here than in any other form of the disease. If the careless use of tuberculin will produce the most harm in acute or active tuberculosis, we have at least this consolation and warrant for persisting in its use: the fact that we cannot do much to increase the seriousness of the condition as it presents itself to us. Again, we can make our plea for tuberculin treatment in these conditions more persistently now that we have a method of

tuberculin administration which has raised the degree of safety to such an extent that it may be safely used in acute conditions. Any general practitioner who has used this method of tuberculin administration in but one or two cases where its use was not very difficult, is qualified to use it in active pulmonary tuberculosis. We have only to classify our cases in order to be able to apply the proper auxiliary treatment. We must be able to recognize the difference between fever due to auto-inoculation and fever due to mixed infection; between hemorrhage due to an ulcerative process and hemorrhage due to trauma that is brought about by excessive coughing; between an afebrile case with an ulcerative process belonging to the active form of the disease and which is afebrile on account of having excellent drainage by being in close proximity to a larger bronchus and an afebrile case which belongs to the chronic and slowly progressive type. By making careful distinctions, we shall have achieved two important aims which will help materially in the success of tuberculin therapy. In the first place we shall have removed many an obstacle to the successful prosecution of a course of tuberculin treatment, by treating symptoms which on closer analysis will be found to be due to other causes than negative effects of the tuberculin. And in the second place, we shall have removed the necessity of expert classification of patients in order to judge whether tuberculin therapy is indicated or contraindicated. This will be a great gain, for, instead of giving so much consideration to supposed contraindications to tuberculin therapy, we shall give closer attention to the treatment of the elements which bring about those contraindications. In this way, we shall do much to remove the mysticism that surrounds tuberculin therapy and in its place discover many details in the condition of our patients. These details have been overlooked as a result of the hopelessness which we have heretofore associated with the acute

A careful distinction as to the cause of temperature and hemorrhage, and a more guarded classification of other symptoms will discover their cause to be other than the tuberculin treatment.

condition, but if accounted for will go far to improve the condition of the patient.

Beginning Treatment. It is quite safe to begin treatment with the fifth dilution in nearly all cases of acute or active pulmonary tuberculosis. There are, however, some exceptions, and these can be placed into two main classes.

The treatment of acute or active phthisis is begun with 0.000001 c.c. of OT, except in cases where the first few inoculations cause distinct local reactions, when the dose should be 0.0000001 c.c.

First, there are those acute cases where the tubercular process is recent, having begun as an acute infection. If after the first few inoculations with the fifth dilution, local reactions are prominent, it may point to the presence of a constitutional reaction which is masked by a high temperature already present as a result of the active process. It is therefore better to go back to the sixth dilution in case of distinct local reactions following the beginning with the fifth dilution.

Second, there are those cases of acute or active pulmonary tuberculosis which are acute exacerbations of a chronic process that has existed for some time. These acute exacerbations are brought about very frequently by mixed infection.

All tubercular affections in the lung indicate beginning treatment with the fifth dilution. However, that may be far from the maximum tolerance, and since it is necessary to reach that maximum tolerance in these cases as soon as possible, it is best to proceed with the dosage by increasing the increase at every inoculation instead of at every other inoculation. For example, the sequence of dosage would be as follows: Solution Number V,—0.10, 0.12, 0.16, 0.22, 0.30, 0.40, 0.52 c.c. and so on. This more rapid increase may be kept up until a *near* reaction is obtained, viz.: a distinct local reaction; distinct focal manifestations; the persistent occurrence of headache after two or three successive inoculations; or any other symptoms that may point to the approach of a constitutional reaction.

The more rapid tuberculin administration is indicated where it is urgent to reach the maximum tolerance.

Conclusion of Treatment. The conclusion of treatment must also take cognizance of the time of the origin of the

acute process, that is—whether it is a beginning process with low resistance,—or whether it is an acute exacerbation of an old process. In the former case, the conclusion of treatment presupposes the checking of the rapidity of the process, and being an early process it would require the simplest conclusion. This means that after OT inoculations are finished, the BE is administered as shown in Table III. For two years after the conclusion of the inoculations of Bacillary Emulsion tri-monthly tests, as described elsewhere, are required.

The conclusion of treatment is much simpler than the beginning of treatment, for once the process is checked, repair is rapid in acute conditions.

Prognosis and Results.

The prognosis in pulmonary tuberculosis, when viewed from the standpoint of immunotherapy, must be considered at three distinct periods in relation to tuberculin treatment.

The first period is when the patient applies for treatment. An examination is made, and a fair knowledge is obtained from a physical examination, a microscopic examination of the sputum, a three-day temperature record, and an X-ray picture of the lungs. These, together with the history of the course of the disease prior to the beginning of treatment with tuberculin, when considered together, form a basis for a fairly accurate prognosis. The history must, of course, take accurate account of the patient's loss of weight previous to this examination—whether it was rapid or slow—whether the present-day treatment, as the hygienic-dietetic and climatic treatment was applied and what effect it produced upon him—whether it was discontinued on account of the failure of the treatment, or whether the patient was impatient and did not give it a fair trial. Again, what are the habits of the patient and his mental attitude towards his occupation? Can the failure of the climatic treatment be attributed to an intense psychic effect, caused by being deprived of his ordinary habits and pursuits? All these elements play a far greater rôle in determining the prognosis of pulmonary tuberculosis than we have hitherto realized; in fact, these factors play just as important a part as the stage

The prognosis at the beginning of treatment must be guarded in all cases and no element overlooked which may have a bearing upon it.

of the disease. To a patient with a fairly advanced tubercular lesion in the lung, who has demonstrated an inability to keep away from his ordinary pursuits, we can offer a much better prognosis with the ambulatory tuberculin treatment than to an incipient case who is willing to submit to the tuberculin treatment through bravado, but is constantly worried that he has probably chosen a hazardous method of treatment and would have done better with a change of climate, etc. We must, in all events, remember that permanent damage will result after destruction of lung tissue and the symptoms remaining after the tubercular process has been cleared up, will be in proportion to the amount of destruction that has taken place before the process has been checked.

Temperature has a great bearing upon the prognosis at the beginning of treatment. If a patient runs a high temperature, prognosis is very difficult until the temperature has been checked or at least its nature determined. If it is due to auto-inoculation, it usually points to a rapid progress with a tremendous hypersusceptibility and consequently makes the prognosis far graver than when the temperature is due to mixed infection. In the latter case, vaccines have been successful rendering the prognosis more hopeful when the temperature is caused by the mixed infection.

Once the tuberculin treatment has demonstrated a positive response, the prognosis, barring intercurrent conditions, may be considered as favorable.

The second period is when the patient has had sufficient tuberculin treatment to demonstrate a response. By this time, a great many doubts which existed when the patient first applied, have been cleared up. The progress of a temperature at the beginning of treatment will at this time make itself evident. We shall know whether the temperature is controllable or otherwise; and if it was due to mixed infection, whether or not it responded to vaccine treatment. A change in the quantity of the sputum, or in its consistency, or in both, will have a decided bearing upon our estimation of the efficacy of the immune response we have been able to elicit. A more decided localization of the physical signs in

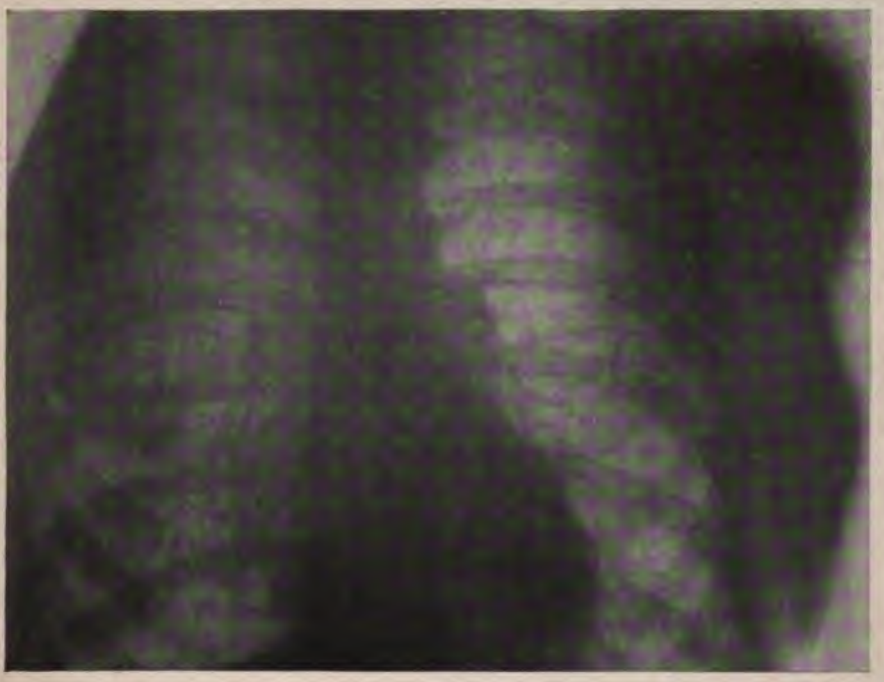


FIG. 35.—A young man, twenty-two years of age, a bank clerk by occupation.

About six months before he came to me for the first consultation, his brother died of pulmonary tuberculosis. He himself was always well, but he had grown very rapidly in height, and became very thin. About three years ago, he had a severe attack of grippe, which was followed by a cough and the presence of tubercle bacilli in his sputum. He went to the mountains where he recuperated and returned after about four months' stay, apparently well. One year and a half ago, he began to cough again, had night sweats, and hectic flush. In spite of the recent death of his brother and the fact that his own sputum was once positive, he refused to take his condition seriously, until I convinced him that it was an active recurrence. Upon the advice of another physician he decided to refuse tuberculin treatment, and went to Saranac Lake, where he remained three months with little improvement. He finally lost patience with the "rest in bed, and with the ever present tubercular patients all around him," and returned to New York City, where he applied for tuberculin treatment at my office.

At this time there were physical signs throughout the right lung, and at the apex of the left lung. Tubercle bacilli in the sputum numbered about fifteen to twenty in a microscopic field.

This X-ray photograph, taken at this time, shows considerable infiltration of the upper two-thirds of the right pulmonary field. The infiltration seems to be of a connective tissue type. The left pulmonary field is clear except for slight clouding (indicating a recent process).

the chest forms an important prognostic element which occurs as a result of effective tuberculin treatment. It indicates the disappearance of inflammatory changes, radiating from the actual point of tubercular infection during the more active tubercular process. This can only point to a favorable response to the treatment and of course it must necessarily improve the outlook for the patient. An improved mental attitude as a result of improvement in the general condition following the first inoculations of tuberculin will point to a better prognosis than perhaps an improvement of greater degree without the mental effect.

A favorable response from tuberculin may become evident early in the treatment, however it may not appear until late in the treatment.

Although tuberculin may elicit a response from the first dose, it nevertheless more often occurs after the maximum of tolerance has been reached. It therefore may require the positive phase following a constitutional reaction before a real beneficial immune response will become evident through the tuberculin treatment. Once a distinct response to the tuberculin treatment is noticed, the prognosis becomes a great deal better, for nothing but an unusual occurrence, such as an unduly severe tuberculin reaction, or intercurrent disease, can stay the favorable progress with tuberculin inoculation once the patient has demonstrated a response.

The prognosis at the conclusion of treatment will depend upon the amount of permanent damage produced by the infection.

The third period is the prognosis at the conclusion of the course of tuberculin treatment. At this point it is not strictly prognosis that we have to consider, but the patient's present condition and its bearing on his future health. What is the amount of permanent damage left behind—how much of the function of the lungs will be permanently interfered with as a result of such damage—how much of the pathological change was brought about by a mixed infection—and how well this mixed infection was under control at the time—all these elements have a great bearing upon the final results we may obtain with tuberculin. If frequent repetition may be pardoned, I will again state that in our expectations regarding the most optimistic results from

tuberculin therapy we cannot overlook the fact that with the removal of tuberculosis as an infection, we do not eliminate the damage resulting from it. Hence the condition of the patient at the conclusion of successful treatment will depend largely upon the amount and position of the pathological changes which have taken place during the life of the infection.

The report of quantitative results obtained with tuberculin in the treatment of pulmonary tuberculosis would have to embody such a large number of cases to make an impression, that it is still beyond my experience to include a sufficient number in this work. For me to attempt a statistical exposition of the results obtained as given in the literature on the subject would be useless for two reasons: First, such statistics may be gathered from almost any work on the subject, as most of the works on tuberculin treatment to be found at the present day consist mainly of statistics and consensus of opinions. Secondly, I have here presented a more simplified and more easily adaptable method of tuberculin administration, which will produce even better results than have been obtained with tuberculin heretofore.

Statistics are superfluous in a "practical guide."

As to the permanency of the results obtained from the treatment of pulmonary tuberculosis with tuberculin—I have laid great stress upon the tuberculin test to be applied to the patient for two years after the conclusion of treatment. This necessarily adds to the results an element of permanency not obtained in former reports. Since it is true that the conclusion of treatment is more or less empirical, just as in the case of the beginning of treatment, there are those cases where the conclusion of treatment may not have gone far enough, and a recurrence of hypersusceptibility may take place. And as it is well known that a recurrence of the hypersusceptibility is a forerunner of the recurrence of the disease, it was found necessary, in order to assure the permanency of the results obtained, to test the patient with tuberculin at certain intervals for a period of time after the

A greater number of permanent cures, and more lasting results are brought about by a more careful conclusion of tuberculin treatment, plus the tri-monthly tests.

conclusion of the treatment. These tests are made in order to determine in which of the cases the conclusion of treatment was not carried far enough. Thus we get ahead of the recurrence of the disease by overcoming the recurrence of hypersusceptibility. That is the reason why the results I have obtained—although quantitatively not sufficient for an authoritative exposé,—can still claim qualitatively a superiority over former results.

Careful attention to mixed infection adds greatly to the permanency of the results.

One more element should be reckoned with in the permanency and frequency of better results obtained,—that is the treatment of mixed infection which is given prominence in this work (see Part III). I am quite certain that with proper attention given to the subject of mixed infection with due consideration to its vaccine treatment, an element will be added to the matter of tuberculin therapy, which will add both quality and permanency to the results obtained.

The feeling of well-being brought about by tuberculin, exerts a good influence on the general condition of the patient.

More important than statistics are the results produced in the various symptoms during tuberculin treatment. These results encourage both the patient and physician. The earliest and most striking effect that is noticed is the sense of well-being on the part of the patient. Granting that the larger part is brought about by "suggestion and auto-suggestion"—it still adds an element which is most important to the favorable progress in the treatment of any disease.

Tuberculin is a distinct anodyne for tubercular pain.

Pain. Tuberculin has a distinct anti-phlogistic action upon pain brought about by a tubercular condition, and will thus be found a great aid in relieving a symptom which causes most of the distress. However, pain produced by pleuritic adhesions occasionally persists even in patients who have noticeably improved, or remained well for years.

Digestion and appetite improve.

Digestion. Both appetite and digestion markedly improve. That may be brought about by the general well-being which is most sedative in its action upon neurotic digestion, or upon the improvement of the general tone of the digestive apparatus.

Weight. The tuberculin treatment must be considered

as having a direct influence upon the weight of the patient. That may be noticed upon the ambulatory patients who cannot change their mode of living in any way. These patients, although they have not gained in weight previous to the tuberculin treatment, gain in weight soon after the institution of tuberculin treatment. And since nothing but tuberculin has been added to the treatment, the result must be attributed to tuberculin. Of course, here again we may attribute such gain to the influence of tuberculin on the general well-being, and to the improvement of digestion.

The increase in weight brought about by tuberculin is always accompanied by increased strength.

Fever. The effect of tuberculin on fever cannot be mistaken. Tuberculin acts as a direct anti-pyretic, and nothing will reduce temperature due to the tubercular infection as quickly as tuberculin treatment. Adverse opinion as to the effect of tuberculin on fever may be attributed to two distinct reasons; first, the failure to differentiate between pyrexia due to tubercular auto-inoculation, and that due to mixed infection or other conditions; secondly, a faulty technic in tuberculin administration.

Tuberculin is distinctly antipyretic in tubercular fever.

Pulse. The influence of tuberculin on the pulse is in direct proportion to its influence on the temperature and general well-being of the individual. If the tachycardia is due to a mild carditis which resulted from a long standing infection, tuberculin will have no effect upon it. It will have to be treated as a heart condition so as not to allow it to dissipate the beneficial effects obtained from tuberculin.

The pulse improves with the other symptoms.

Cough. Cough may be increased as a result of the focal reaction accompanying the tuberculin treatment, but it is rendered less irritating and less strenuous. Later, as the effect of the tuberculin treatment becomes cumulative, the cough diminishes. This is especially true of the dry and irritating cough. Careful attention must be given to cough originating from other sources than the tubercular process, such as naso-pharyngeal conditions, mixed pulmonary infections, etc. Many a patient has lost patience with the tuberculin treatment because of the persistence of an annoy-

Cough is diminished, and becomes less irritating.

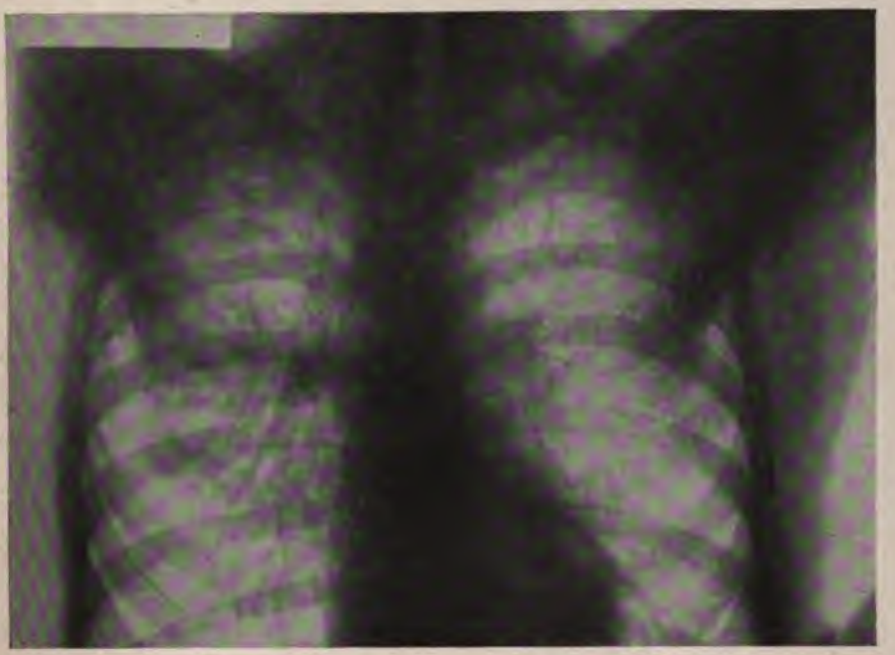


FIG. 36 shows an X-ray photograph of the chest of the same young man* ten months later, at the conclusion of a successful tuberculin treatment. The infiltration has greatly diminished, the clouding has disappeared, while the apices alone show signs of a former tubercular lesion (permanent damage). For the past five months there have been no tubercle bacilli in the sputum, there is rarely any cough and the patient has been able to work ninety per cent. of the time during his tuberculin treatment.

* As Fig. 35.

ing cough after months of tuberculin treatment. The physician should demonstrate this cough as originating from a condition quite apart from the tubercular process, and treat it as such without interrupting the tuberculin treatment which was producing the desired effect on the tubercular process.

Hemoptysis. The general belief that tuberculin will produce pulmonary hemorrhage or even increase hemorrhage when already present, is based upon a fallacy born of prejudice. Tuberculin does not tend to produce hemoptysis. On the contrary, it will slowly diminish and finally permanently stop recurrent hemoptysis.

Tuberculin exerts a beneficial effect on hemoptysis.

Expectoration. The amount of expectoration may increase at the beginning of tuberculin treatment, but the consistency of the sputum will reveal a beneficial effect. The sputum becomes thinner and is more easily brought up. The microscopical change in the sputum has not escaped the notice of any physician using the tuberculin treatment. The diminution in the number of tubercle bacilli is striking, followed by a more rapid and more frequent disappearance of the tubercle bacilli, than with any other form of treatment. Even in hopeless conditions, a disappearance of the tubercle bacilli from the sputum may be accomplished with the tuberculin treatment. This fact alone offers sufficient argument for the use of tuberculin in patients that are hopeless as far as a cure is concerned.

The tubercle bacilli will more frequently disappear from the sputum during tuberculin treatment than during any other treatment.

Physical Signs. The physical signs are modified by tuberculin treatment in proportion to the amount of permanent damage produced before the immune response became sufficient to check the infection. Since scar tissue, distorted lung structure, calcareous infiltration, constriction of bronchial tubes, etc., will produce physical signs, it stands to reason that such signs will persist, for any or all of these pathological changes form part of the healing process. Of course in early incipient cases all physical signs may disappear. When Tripier said that once a tubercular lesion

Only such physical signs persist as are produced by the distortion of the lung tissue during the healing of the disease.

in the lung presents physical signs, the lesion is incurable—he really referred to the permanent damage,—lung tissue never reforms,—scar tissue must take the place of the destroyed lung and thus change the normal physical signs.

Fibrosis—the best form of healing in tuberculosis—is usual in tuberculin treated patients.

Pathology. The consensus of opinion throughout the literature as to the difference in the pathological changes in tuberculin treated patients and those treated without tuberculin, seems to leave no doubt that fibrosis occurs far more frequently in the former than in the latter. This fact offers another important reason for the use of tuberculin, for scar tissue formation is in the nature of all healing processes. It therefore offers a more lasting effect than any other form of healing.

Roentgenography has an important field in pulmonary tuberculosis, and should be far more generally used.

X-ray Findings. A wider adoption of Roentgenography in pulmonary tuberculosis in recent years has become a great aid in the determination of results of tuberculin treatment (or of any other treatment in pulmonary tuberculosis). Whereas the pathological findings had to be determined at autopsy and therefore had a more or less theoretical bearing upon the results of tuberculin treatment as compared with other treatments, the findings as shown by X-ray examinations are applicable to all stages of the disease. In these stages are included the more important class of cases that come under the arrested or healed conditions.

Roentgenographic findings are of great aid in prognosis.

Important contributions to the X-ray studies of lung structure, such as come from Kennon Dunham and others, by which we may determine the method of healing and the progress of healing of the tubercular processes in the lung, will become the greatest aid to the wider adoption of tuberculin in the treatment of pulmonary tuberculosis. Although this matter is yet too new to allow definite conclusions, it merits the attention which I wish to draw to it at this time. My personal experience has made me most enthusiastic. I would no more think of neglecting an X-ray examination of the chest, both at the beginning and at the conclusion of tuberculin treatment, than I would treat a patient with

FIG. 37.—Radiographic picture of the lungs of the same patient, whose temperature chart is here reproduced (Fig. 31, page 143).

The lesions in the lungs followed several extensive operations for tubercular glands of the neck. The last operation extended into the supraclavicular space almost exposing the pleura over the apex of the lung. As may be seen in the above X-ray photograph, the lung on the same side (right) is infiltrated and clouded throughout the upper two-thirds of its extent. The left lung seems clear.

tuberculin without a temperature record. I have included Figures 35, 36, and 37 to emphasize my purpose in calling attention to this subject. Not only are such demonstrations as shown in these illustrations helpful and gratifying to the physician, but the psychological effect on the patient alone merits the trouble and expense that an X-ray photograph may entail.

Chapter VII

MISCELLANEOUS TUBERCULAR CONDITIONS

There are very few instances of tubercular infections, aside from those we have described in the foregoing chapters, which are not complications or extensions of the more important processes we have already described. However, since few of these processes may exist alone or are so prominent when they come to our notice—the original process having become arrested—special attention must be called to their treatment. The following are the conditions which need special mention.

Tuberculosis of the Pleura

In acute pleurisy it is best to discontinue the tuberculin treatment until the acute symptoms are over.

The tubercular infection of the pleura exists mostly as a complication of pulmonary tuberculosis, and need not be considered, as far as tuberculin treatment is concerned, apart from the pulmonary process. It is only necessary to mention at this point that when pleurisy in an acute form, with temperature, suddenly complicates pulmonary tuberculosis, it is best to wait for the subsistence of the acute symptoms and the temperature before specific treatment is begun. And when it occurs as a result of an acute infection, such as influenza, etc., during tuberculin treatment, it is best to discontinue the inoculations until the acute symptoms are over.

Idiopathic tubercular pleurisy rarely exists—hence it should always be treated as a pulmonary lesion.

The so-called idiopathic pleurisy is getting to be recognized more and more as a complication of an undiscovered or latent pulmonary tubercular process. So frequently has pulmonary tuberculosis appeared in a patient some time after an attack of the so-called idiopathic pleurisy that most authorities are now recognizing idiopathic pleurisy as tubercular in nature, and secondary to a pulmonary lesion. These facts, when once appreciated, make the indications for tuber-

culin therapy in pleurisy a great deal clearer. Hence, the tuberculin treatment of pleurisy, where pulmonary lesion cannot be discovered, would certainly be the most rational treatment, as it implies early pulmonary involvement.

In the case of temperature accompanying pleurisy as in the case of pleurisy complicating a definite pulmonary lesion, it is best to wait for a subsidence of temperature before tuberculin treatment is begun.

The beginning and conclusion of treatment of the so-called idiopathic pleurisy is the same as that outlined for incipient pulmonary tuberculosis.

Tubercular Peritonitis

Tubercular peritonitis is another form of tuberculosis which cannot be said to be primary in nature. In all probability it is most frequently an extension from the mesenteric glands. The value of specific treatment in this condition is no longer doubted, as all authorities, who report on the use of tuberculin in peritoneal tuberculosis, agree as to its therapeutic value. In this connection, we cannot overlook the favorable effect on a tubercular process in the peritonem, of the exposure of the peritoneal cavity to the air by means of laparotomy. The effect of this procedure has been so frequently noted that we cannot doubt its effect. However, a great many cases are not improved and some even become distinctly worse after laparotomy; and in these cases, tuberculin remains the only means of effective therapeusis. Again, we may have tubercular peritonitis complicating extensive lesions in a bone and joint, lung, and wide-spreading glandular involvements where laparotomy would be contra-indicated, but where tuberculin administered for the major conditions has shown a marked effect in the peritoneal condition. Barring such cases of tubercular peritonitis, which are discovered only through laparotomy, it is simpler and more effective to treat peritoneal tuberculosis with tuberculin.

Tuberculin is of value in tubercular peritonitis to remove the source of the infection in cases where laparotomy has brought about a cure, and to effect a cure in cases where laparotomy proved unsuccessful.

Even those conditions which clear up after laparotomy could be benefited by tuberculin, by reason of the influence which it exerts over the original focus of the disease. The following three cases will illustrate effectively the value of tuberculin in peritoneal tuberculosis. The first represents the type of case that recurs in spite of laparotomy. The second illustrates the value of tuberculin in extensive peritoneal involvement with an extension of the tubercular process following laparotomy. It proves the conclusion that even if the local peritoneal region is improved as a result of the laparotomy, the tubercular infection as a constitutional disease still persists and may progress unfavorably. The third shows the value of tuberculin in peritoneal involvement, including involvement of the stomach wall and intestines, with extensive constrictions and angulations which could not all have gotten well by laparotomy alone, even if the laparotomy which was attempted before the tuberculin treatment had succeeded.

Example: Successful tuberculin therapy in a case of repeated recurrence after laparotomy.

CASE I. A full history of this case may be found in the chapter on Treatment of Glandular Tuberculosis, page 76. It shows a patient on whom a laparotomy was performed for tubercular peritonitis, and in spite of the exposure of the peritoneal cavity to the sun and air, the peritoneum did not recover from the tubercular process. The chronic symptoms continued through a period of two years, finally culminating in acute peritonitis, with tubercular ulcerations of the appendix. Even after the final laparotomy, the signs of chronic peritonitis continued until tuberculin was administered.

CASE II. A little girl, six years of age, had a negative family history. She lived in a region where the milk supply was found to be from a tubercular herd. Hers was a case of malnutrition from the beginning. Until she was four and a half months old, she did not gain in weight at all. At the age of three she began to be fussy and whiny. She had a poor appetite, and was always too tired to play. She

grew worse and had a temperature rise every night, and also night cries. The doctor who examined her found a mass in the region of the appendix. She was taken to the hospital for appendectomy. At the operation the appendix which was removed looked normal, but a mass of enlarged glands was discovered in the retrocolic region. Her recovery from this operation was slow. Soon after there was a noticeable enlargement of the glands of the neck, both cervical regions being affected. Tuberculin treatment was advised and carried out according to my technic. Two months after the beginning of treatment the child's weight was 34 pounds. This was a considerable increase over her weight at the beginning of treatment, the definite amount of which was not noted. She responded to the tuberculin treatment from the beginning, and by the time the conclusion of the treatment was reached, she had gained fourteen pounds more. The tubercular glands in the neck and the abdominal symptoms entirely disappeared.

Example: Laparotomy with a complete disappearance of the tubercular peritonitis but followed by an extension of the process elsewhere—requiring tuberculin therapy.

CASE III. A girl, nineteen years old, came frequently to my clinic with a little nephew who was being treated for wide-spread tubercular lesions. At one of the visits she asked whether she could get any help for herself, and apologized for speaking of herself because she was not a tubercular case. I became interested in her condition, and thought I would establish a diagnosis and then direct her for proper treatment.

Example: Successful tuberculin therapy in general peritonitis with extensive involvement of the gastro-intestinal tract—where laparotomy was impossible.

She had always been healthy except that her menstrual periods had never become established on a normal basis. Her menstruation was scant, and came at long intervals the first few years, and disappeared entirely for three years previous to this consultation. Her chief complaint was constant vomiting—not a day for two years was she free from vomiting, with general pains in the whole abdomen and frequent attacks of cramps. The whole complexity of symptoms as she presented them, seemed to point to pyloric obstruction. There was no history of hemoptysis, but the

patient had lost a great deal of weight in the last two years. An X-ray study of her gastro-intestinal tract revealed a typical hour-glass stomach. (Fig. 38.) On palpation I found that the lower half of the abdomen seemed to be filled with a hard tumor, reaching to about one finger's breadth above the umbilicus. A preoperative diagnosis was, "hour-glass constriction of the stomach due to ulceration, and a large fibroid tumor of the uterus."

Under general anesthesia, laparotomy was performed with a right median incision reaching from the ensiform cartilage to the umbilicus, in order to first reach the obstruction and to relieve it by gastro-enterostomy if necessary. The abdominal cavity was never reached. Layer after layer was cut through—there seemed to be no end to the layers of peritoneum. The attempt had to be given up. The mass of membraneous tissue seemed now to be intimately connected with the bowel omentum and stomach, so that entrance was made impossible. It was decided to remove at least the tumor, and a second incision was made below the umbilicus. The skin and facia were incised, and one rectus muscle pulled to one side. Instead of peritoneum, a layer of cartilage was discovered—the peritoneum seemed to have been converted into cartilage. The tubercular nature of the peritoneum became apparent, and so the attempt to enter the peritoneal cavity was abandoned. Although I was fully conscious of the beneficial results that would be brought about by opening the tubercular peritoneum, it was decided not to do so in this case for fear of an eventual inability to close the peritoneum.

The patient made an uneventful recovery from the surgical interference, and two weeks later was put on tuberculin treatment. After the ninth inoculation, improvement in the symptoms began. The vomiting spells became less and less frequent. Treatment was begun with the fourth dilution and by the time the second dilution was reached, the vomiting and pain disappeared entirely. The patient

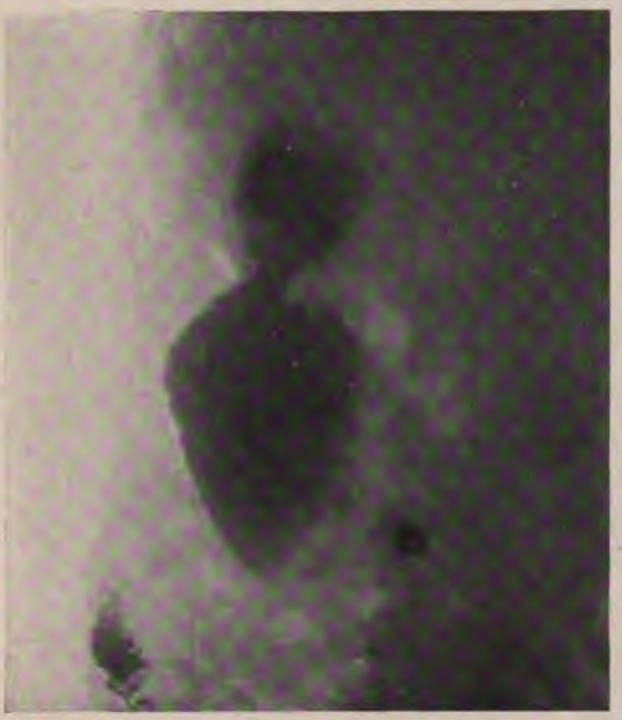


FIG. 38.—X-ray photograph of the stomach, showing hour-glass constriction due to tubercular ulcerations and adhesions. The symptoms due to the condition were all relieved by tuberculin treatment. (See case III, page 138.)

had gained about eleven pounds in weight, and strange as it may seem, the hardness of the abdominal wall, which was thought to be a fibroid and was found to be due to the cartilagenous peritoneum, began to soften. At the end of treatment with tuberculin, the abdominal wall felt entirely normal, and the patient is now in apparent perfect health.

Extensive accumulation of fluid should always be withdrawn by small incision or puncture or aspiration, whether it occurs immediately before the tuberculin treatment is begun, or whether it occurs during tuberculin treatment. A course of OT, beginning with the fourth dilution—and in very young children with the fifth dilution—is usually sufficient to cure a case of peritoneal tuberculosis. We may conclude the treatment with Bacillary Emulsion or not, as the case may be. That may be left to the discretion of the physician. However, if there is an evident focus from which the infection came, it is best to conclude the course of treatment with Bacillary Emulsion.

Tuberculosis of the Eye

The effect of tuberculin in tubercular involvement of the eye was responsible for my early enthusiasm for the value of tuberculin in general. To quote from Bandelier and Roepke, "Tuberculin has brought about such triumphs in ophthalmic practice as to call increasing attention to specific treatment, and in this field a considerable contribution was made towards rescuing the reputation of tuberculin. The surprising cure of the severest forms of ocular tuberculosis, vision being retained without the assistance of any other therapeutic measure, is in fact so striking as to exert a *healing effect also on the blindness of the opponents of tuberculin.*"

Tuberculin is the therapy par excellence in any tubercular involvement of the eye.

But even here a measure of care must be exercised in the tuberculin administration. As universal as the beneficial effects of tuberculin in ocular tuberculosis have been (see the large amount of literature on the subject), bad

results may nevertheless be produced with a faulty technic. The following is a good example of the ineffectiveness of tuberculin treatment when administered by too slow a technic, even though the patient was treated in a sanatorium which was the pioneer institution for the use of tuberculin in this country.

Example: Showing that an improper technic may prevent favorable results even in ocular tuberculosis

A young man, twenty-five years of age, at first had keratitis in one eye, which soon after spread to the other eye. He was treated by one of the most prominent oculists in New York for a number of years. Owing to the stubbornness of the lesion the patient was sent to Saranac Lake, in the Adirondack Mountains, New York, where he was treated with tuberculin over a period of two years. In spite of this treatment, his condition grew worse, so that by the time he returned to New York City he had retained but ten per cent. of his field of vision. The oculist who had a prejudice against tuberculin previous to the patient's visit to the Adirondacks, had his opinion strengthened by the failure of the tuberculin in this case.

It was therefore through a special circumstance that the patient came to my clinic in the New York Polyclinic Hospital for treatment. He brought with him an accurate chart of the tuberculin treatment which he had received at the Adirondack sanatarium. It showed treatment with Bacillary Emulsion—the dosage so minute, that if anything, it would have encouraged an increase in hypersusceptibility. I commenced treatment with the fourth dilution of OT. A mild reaction occurred after the tenth inoculation. The improvement in his tubercular condition was so marked that after two months of treatment he dared to tell the oculist that he was being treated in my clinic—a thing he was keeping secret lest he would lose the friendship and treatment of the oculist, whom I encouraged him to visit regularly for the local treatment. By the time we concluded treatment with tuberculin, his field of vision had increased to seventy per cent,—seven times the amount of vision that he had at

the beginning of tuberculin treatment. Both through the constitutional improvement due to tuberculin, and through the mental exhilaration, his general improvement kept pace with the improvement in the local condition. His trimonthly tests proved negative and he is now discharged cured.

The following three points, brought out by this history, more than emphasize the falsity of the premise that governs the prejudice against tuberculin. They also show how easily other elements and not the tuberculin itself may intensify such prejudice:

First, the oculist, who is now converted to a favorable attitude towards tuberculin, has acknowledged that his prejudice was based on nothing but hearsay, and that he had never had a personal experience with its use.

Second, the tuberculin treatment at first failed in this case—not because of an inefficiency of tuberculin,—but because of a faulty technic in its administration.

Third, the publication of such negative results from the tuberculin treatment, coming from such an authoritative source as that particular sanitarium, does more to prevent the wider adoption of the use of tuberculin than any other agency.

Beginning and conclusion of treatment.

The beginning treatment of eye tuberculosis where the involvement is acute and extends to the interior of the eyeball should be with the fifth dilution. But where the disease is limited to the conjunctiva, cornea, iris and so on, 0.10 c.c. of the fourth dilution is not too large a beginning dose. It is best to conclude the treatment with Bacillary Emulsion as shown in Chart III.

Tuberculosis of the Ear

Tuberculosis of the ear is known to be favorably influenced during the tuberculin treatment of other conditions.

The literature is very meager as to the effect of tuberculin in tuberculosis of the ear. My experience consists of ear involvements in two cases of pulmonary tuberculosis, and in one case of renal tuberculosis. In all three, the ear conditions cleared up during the tuberculin treatment.

Tuberculosis of the Skin

Lupus offers one of the most fertile fields for the use of tuberculin. The skin specialists have long since noticed the absolute necessity for constitutional treatment in all refractory skin conditions. Can there be a more perfectly adapted constitutional treatment than tuberculin for the skin lesion which is tubercular in nature? Tuberculin will overcome deep-seated induration; and in those cases where the lupus spot does not entirely disappear after the tuberculin treatment, the various forms of local treatment such as pyrogallic acid, Finsen treatment, etc., will find their proper places. As Wolters puts it, "The exciting cause of the disease seems to be enticed from the body and given out by exudation, and is then destroyed by pyrogallic acid." In lupus of the mucus membranes where these local treatments are impossible, or of no value, tuberculin will show its best effect.

The local treatment of lupus can prove of value only when combined with the constitutional tuberculin treatment.

Since the large percentage of lupus occurs in individuals suffering from other forms of tuberculosis, especially that of the lung, we have to divide the tuberculin treatment into two distinct methods—the reactive, which applies to lupus appearing alone—and the method of tuberculin treatment, applying to the various forms of the infection which the lupus complicated. In other words, if lupus appears in combination with, or as an extension of tuberculosis of the glands or of the lungs,—the tuberculin treatment will apply to the glands or to the lungs, and the lupus condition will take care of itself as a result of the treatment of the other condition. The treatment, however, of primary lupus is entirely different. Here the reactive method will show the best result. The severe focal reaction that takes place with the constitutional reaction will help to throw off the diseased tissue; and as a result, scarring over and healing will soon take place. Beginning the treatment with 0.10 c.c. of the second dilution, this dose is increased, and the increase is increased at every inoculation, instead of at every other inoculation, until a constitutional reaction occurs. The dose

The reactive method of tuberculin therapy is best in lupus.

which produced the constitutional reaction is now repeated until it no longer produces a constitutional reaction. The only change we make as a result of these reactions is to make the interval a week, instead of bi-weekly, as before the constitutional reaction. After the dose no longer produces a reaction, we again inoculate bi-weekly, increasing the dose as at the beginning of the treatment. Should these constitutional reactions affect the patient too severely, the dosage should be increased more slowly after the constitutional reaction by following the same indications here as we do in the treatment of the other conditions. (See Table II.) The conclusion of treatment must be followed very carefully by the rapid Bacillary Emulsion inoculation. (Table III.) The local treatment can be undertaken simultaneously with the Bacillary Emulsion inoculations.

The local treatment of lupus with tuberculin is of no value.

The local treatment of lupus with tuberculin, whether by inoculation into the lupus spot or by inunctions of various other ways, cannot be recommended. As tuberculin depends upon its action on a constitutional effect, the favorable results produced by this method in the few cases that are reported in the literature may have been brought about by a sufficient absorption of tuberculin into the circulation, that amount accidentally being in sufficient quantity to produce favorable results. As a routine, it cannot be recommended for the same reason that the oral administration of tuberculin cannot be recommended—it lacks a most important essential in tuberculin treatment—exactness of dosage.

CHAPTER VIII

SPECIAL CONDITIONS

In concluding the section on tuberculin treatment, I wish to call attention to a few special conditions and irregularities that may arise during the treatment of any tubercular condition with tuberculin.

Constitutional Reaction

A proper differentiation of a rise in temperature due to a constitutional reaction from a rise in temperature due to any other cause is important.

At times it is important to determine whether a temperature rise occurring the day after a tuberculin inoculation is due to a constitutional reaction, or whether the rise is due to factors other than the tuberculin. Any condition that could bring about a temperature rise could just as easily attack an individual the day after a tuberculin inoculation as at any other time. It has been my experience that on many occasions a rise of temperature to 101° F. or higher, which occurred on the day after the last inoculation was found to be due to an intestinal derangement following a dietary indiscretion, a fact that was determined only after careful questioning of the patient. The fact that there was no local reaction and the fact that the temperature persisted longer than one day, or either of these facts alone, was sufficient to arouse my suspicion as to the true cause of the temperature. If questioning the patient does not definitely clear up the doubt as to the source of the temperature, we may resort to the expedient of administering the same dose a second time. This will have a two-fold advantage. In the first place it will verify the fact that the temperature rise was a reaction by producing a temperature again. And in the second place, if the second inoculation will produce no temperature rise, it will avoid a reduction in dose and a slowing of the increases. Colds, mixed infection and many other conditions coming after a tuberculin inoculation may

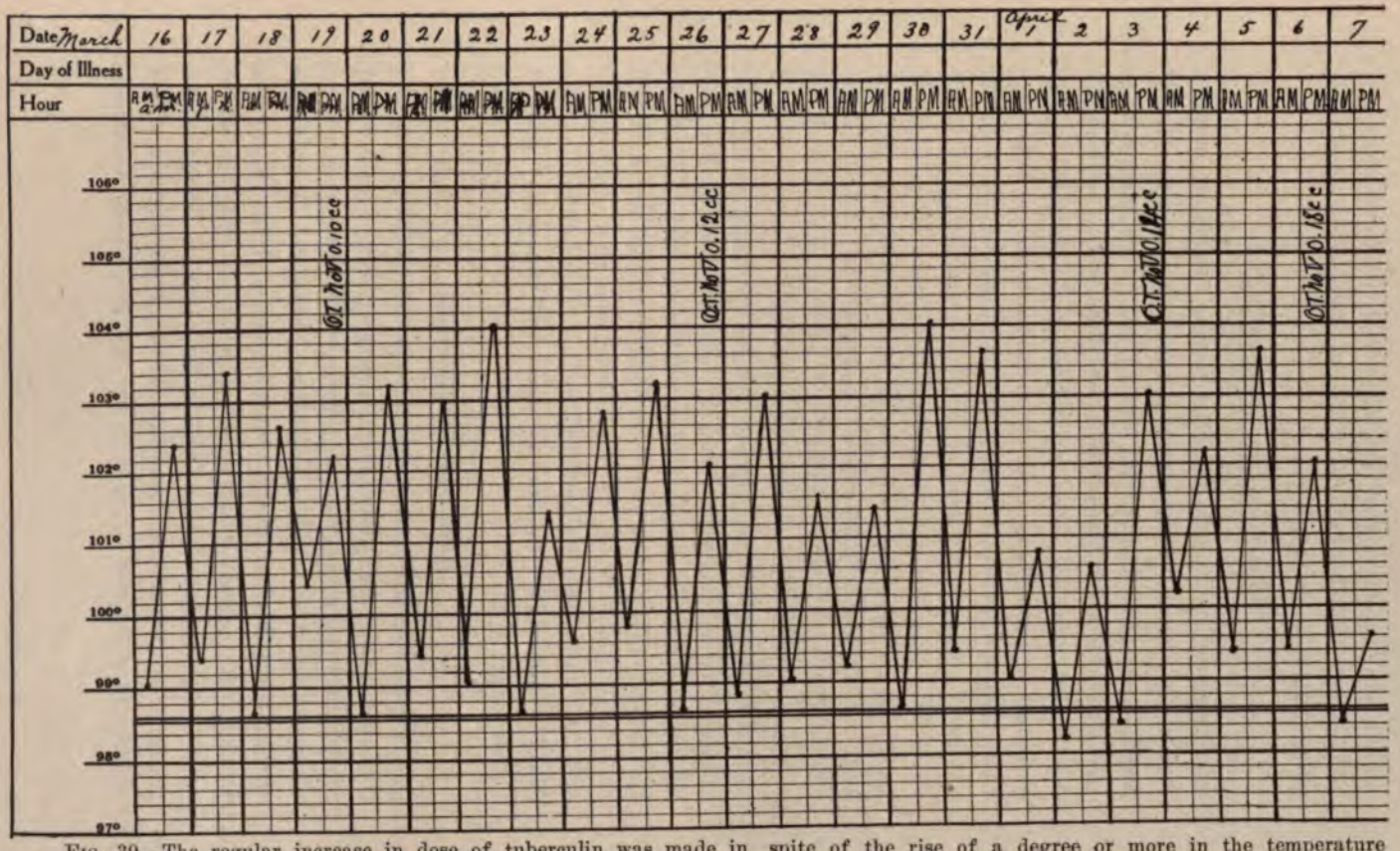


FIG. 39—The regular increase in dose of tuberculin was made in spite of the rise of a degree or more in the temperature after the first three inoculations. The rise in each case was not considered a tuberculin reaction owing to the absence of a local and a distinct focal reaction. This conclusion proved correct after the fourth inoculation by the rapid fall to normal of the temperature which had persisted for months.

simulate a constitutional reaction, but must be carefully recognized in order not to affect the tuberculin treatment. (Fig. 39.)

Tuberculin Intolerance

Occasionally it may happen during the administration of OT that after a constitutional reaction, any dose of OT, however small, will produce a reaction. This phenomenon is distinct from reactions caused by increased hypersusceptibility; for whereas, after an increased hypersusceptibility a change in the variety of tuberculin will make no difference as to the production of a reaction, provided a corresponding amount is used, in the case of intolerance a change of tuberculin will stop the reactions, even if a much larger dose is used. It is therefore necessary in case of a sudden appearance of tuberculin intolerance, to change the variety of the tuberculin used. For example, if after a few months of treatment with OT, a tuberculin intolerance arises, and if at that time the second dilution was being administered, OT is discarded at this point, and a third dilution of BE substituted. The treatment is then continued with the BE in the same manner as it would have been administered if OT were still being used. On reaching the first dilution of BE, the treatment is concluded in the usual manner as per Dose Table III, depending upon the tubercular process under treatment.

The occurrence of tuberculin intolerance may be overcome by a change in the variety of tuberculin used.

Abscess Formation

It was observed early, that the tubercle bacillus cannot be absorbed from the subcutaneous tissue when administered in the form of a vaccine, and when so administered lead to abscess formation. Thus it became necessary to pulverize the bacillary bodies in the manufacture of BE. However, it even now frequently happens that after the administration of BE pure, suppuration takes place around the point of inoculation, with final breaking down of the tissues. The abscess thus formed is more in the nature of a cold abscess,

The more concentrated doses of BE are apt to produce abscess formation at the site of inoculation.

as repeated cultures of the pussy looking fluid that escapes have failed to produce any growth. As such abscesses break down by virtue of a tryptic digestion, healing takes place immediately upon the emptying of the abscess cavity. I have found that diluting the dose two or three times with normal saline, and inoculating the amount in two or three different places at one time, will avoid abscess formation. For example, if 0.20 c.c. of pure BE is the amount to be inoculated, 0.40 c.c. of normal saline can be drawn into the syringe with the 0.20 c.c. of pure BE, the syringe thoroughly shaken, and about 0.20 c.c. of the contents inoculated in three different places, as far apart on the arm as possible.

Autoinoculation

The physical production of autoinoculation should be avoided as far as possible.

I wish to draw special attention to autoinoculation, both in order to distinguish it from tuberculin intolerance, and by way of warning against its artificial induction. Autoinoculation may be brought about by any means which forces an undue amount of the tubercular material into the circulation from the localized tubercular process. An undue amount of breathing exercise may bring about an autoinoculation from a pulmonary lesion. The use of a joint which is the seat of a lesion may force tubercle bacilli or the product of tubercle bacilli into the circulation. Massage over a tubercular area may bring about the same result. This is especially true of knee joint disease.

Example: The production of severe autoinoculation through massage over the infected area.

The following is an interesting example of autoinoculation: A man, forty years old, had a very severe active lesion in the knee joint. After nearly a year in the hospital under the usual orthopedic treatment, a resection of the knee joint was advised. This alarmed the patient, who insisted on going home. After he had been at home for several months, I was called to see him. I found him wasted and pallid, with the entire right leg swollen to twice its natural size. The knee was inflamed and the entire adductor region was a mass of hard induration. The pain, especially with the

slightest movement, was agonizing. The least motion with his toe, the shaking of the bed put the patient into a quiver of pain. The severest ordeal that the patient had to go through was on being removed to the hospital. Four months of tuberculin treatment at the hospital was sufficient to bring about a quiescent state in the lesion,—the surrounding induration, pain and tenderness disappearing,—so that we were able to send him home on crutches. The tuberculin treatment was continued at his home by one of my associates.

After four weeks of treatment at home, and after several doses of the first dilution had been administered, a reaction occurred, which was unduly violent, temperature reaching 105° F. On account of the violence of the reaction, a much greater reduction in dose was made than is customary after a reaction, and again a temperature of 104° F. occurred following the inoculation. A still greater reduction in the dose was made after the second reaction, and a third equally violent reaction occurred. A dose of 0.10 c.c. of the fifth dilution was administered after the third reaction, but still a temperature rise to 105° F. occurred following this dose. It puzzled the attending physician a great deal; he called me into consultation. An examination of the patient disclosed nothing that would account for the increase of the hypersusceptibility. The local condition, in spite of the various reactions, had not become worse. I closely questioned the patient, insisting on an account of his actions for every moment of the day, from his getting up in the morning to his going to sleep at night. After a great deal of cross questioning, the fact was brought out that on the same day that the doctor called to give him his tuberculin treatment, a friend of his, who is a masseur by profession, called on him, and administered a body massage, with particular emphasis on the diseased knee. This was done in a friendly spirit, and " in order to improve his circulation." That it might produce harm was so remote from the patient's mind that he neither mentioned these massages to the physician treating him, nor to me. The mas-

sages were discontinued, and upon my advice 0.10 c.c. of the second dilution—a thousand times the dose which supposedly produced the last reaction—was administered without the least sign of a reaction. In the next four or five treatments the same amount was reached that was administered when reactions began. From there on the treatments were continued uninterruptedly. In about a month from that time he came to the Out-Patient Department of the New York Polyclinic Hospital, for conclusion of treatment, making his bi-weekly trips without any trouble. In less than a year from the beginning treatment, he returned to his occupation as baker.

The only way to overcome autoinoculation is by reducing the activity of the part affected. In febrile pulmonary tuberculosis, rest in bed will reduce temperature if it is caused by autoinoculation.

Tri-monthly Tests

Periodic treatment. tuberculin tests after the conclusion of tuberculin

To one who has had a large experience in the tuberculin treatment of tubercular conditions, the following important fact is evident: any recurrence of the process after it has been arrested during the tuberculin treatment is accompanied by a recurrence of hypersusceptibility. It occurred to me some years ago to follow up the treatment of a series of patients after the conclusion of tuberculin treatment to determine at intervals by a tuberculin test any tendency for the recurrence of hypersusceptibility. I thus found that the recurrence of hypersusceptibility precedes the recurrence of a tubercular lesion. A series of tuberculin inoculations was instituted in every case that showed a recurrence of hypersusceptibility. As a result no recurrence of a tubercular lesion took place in the last few years that these tests were carried out.

The systematic tri-monthly tests were adopted as a consequence of these findings. By applying tuberculin test every three months, for two years followin conclusion of tuberculin treatment, we were al

possible recurrence in all cured cases. A dose consisting of 0.10 c.c. of the first dilution of OT (0.01 c.c. of OT pure) is administered as a test in all cases except where there was a definite history of an infectious disease having attacked the patient between the conclusion of the treatment and this test. If an infectious disease did intervene the divisional method of testing should be adopted; that is, 0.10 c.c. of the second dilution is given as a first test; 0.50 c.c. of the second dilution forty-eight hours later; and then 0.10 c.c. of the first dilution as a final test, forty-eight hours after the second test.

Appropriate tuberculin treatment to overcome recurrence of hypersusceptibility will prevent a recurrence of the disease.

Should any of the tests prove by a constitutional reaction that hypersusceptibility has returned, the patient should again be put on the tuberculin treatment, beginning the course with a tenth of the quantity of tuberculin which caused the reaction, and concluding in the same manner as in the original course of treatment.

The following cases will illustrate the importance of the tri-monthly test in the detection of recurring hypersusceptibility, and the value of treatment to prevent recurrence of the disease where the test is positive.

Example: The recurrence of hypersusceptibility in a case clinically cured.

CASE I. A young man twenty-four years of age, had a negative family history, with the exception of a sister who had tubercular adenitis. His past history showed that he had had measles and chicken pox some time before he was ten years old. Otherwise he was well and strong until five years before the beginning of treatment. At that time he began to have attacks of cramps in the abdomen, which began at the pit of the stomach, radiating and finally settling in the region of the appendix. Nausea and vomiting, followed by diarrhea, would frequently accompany these attacks, which recurred every three or four months, and would last from one to four days. On account of the absence of rigidity over the appendix, a definite diagnosis of appendicitis was not made, but he was treated for "stomach trouble and inflammation of the bowels." In September, 1915, an attack

occurred which was more severe than usual, lasting a week. Another attack followed in October, which persisted for ten days. At this time an operation for appendicitis was advised and carried out in the early part of November. At the operation the tubercular nature of the trouble was discovered. The tubercular process existed not only in the mesenteric glands, but also in the pelvic, peritoneal, and prostate glands. Five days after the operation, severe pain began in the rectum, and after the patient had been kept under the influence of morphine for several days on account of the severity of the pain, the pain suddenly disappeared on the appearance of a large amount of pus in the urine.

After a stay of about three weeks at the hospital, he was referred to me for tuberculin treatment, which was begun on December 11, 1915, and ended on September 14, 1916. During the course of treatment he had only two constitutional reactions. His weight at the beginning of treatment was 148 pounds, which was far below normal weight for his height, and increased to 175 pounds at the conclusion of treatment. The pus in the urine, and the pain in his back and rectum disappeared. Only one attack of abdominal pain occurred soon after beginning the tuberculin treatment, and has never since recurred. Six months after the institution of tuberculin treatment, he returned to his occupation, and has kept at it since.

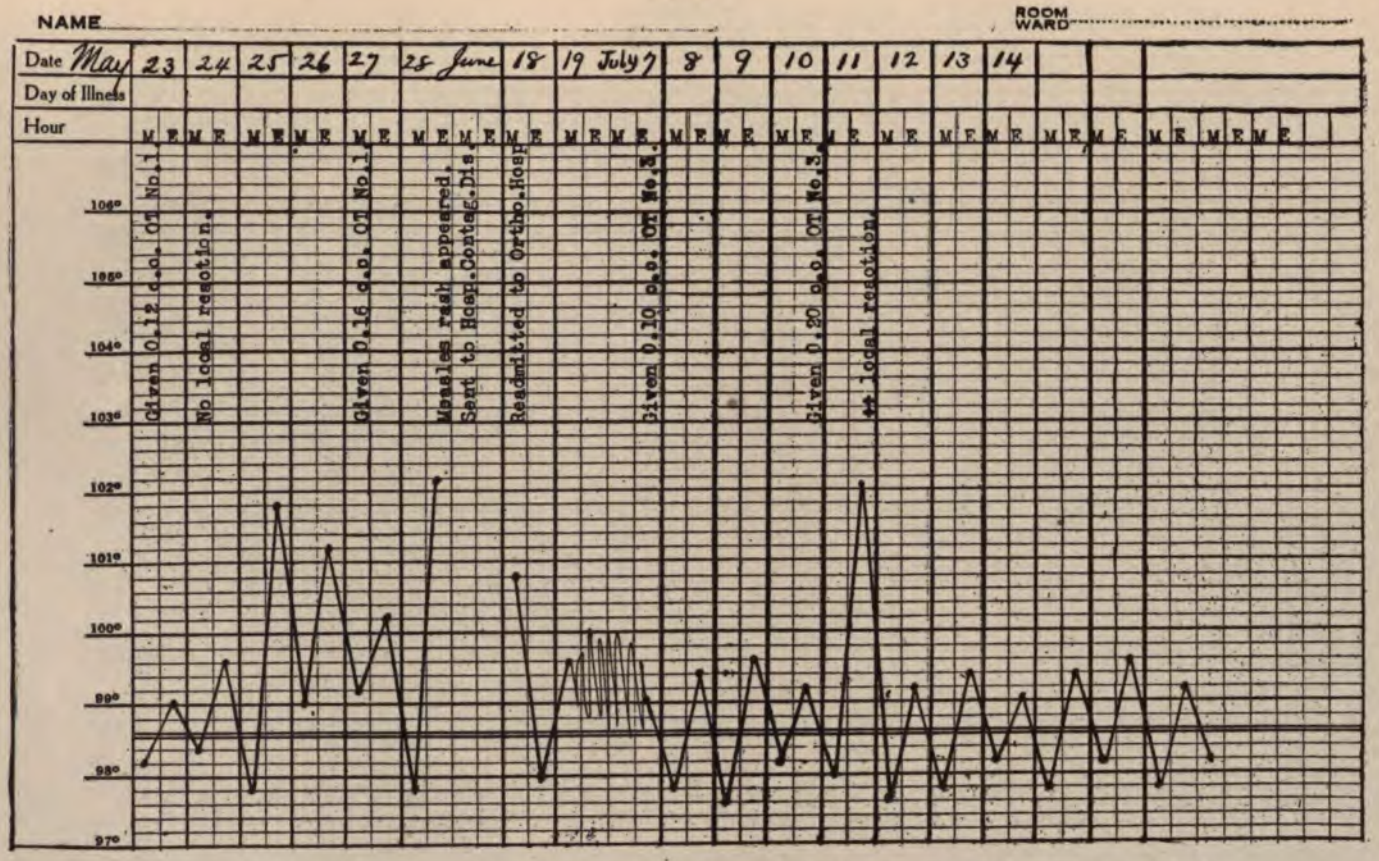
He received the first tri-monthly test in December, 1916. The dose was 0.10 c.c. of the first dilution, and was followed with negative results. The second test was given in March, 1917, and to the surprise of both patient and myself, there was a severe constitutional reaction, the temperature rising to 101° F., pain in the abdomen and in the back being quite severe during the rise in temperature. This patient seemed to have so thoroughly gotten over his disease that I was not at all insistent about his coming for the tests. But as he put it, "the dread of the return of the disease was so strong that he would not miss a single direction given him during

treatment," and so he came punctually for the test. The reaction which followed the second test occurred as the result of 0.10 c.c. of the first dilution. His treatment was resumed with 0.10 c.c. of the second dilution.

Example: An undiscovered recurrence of hypersusceptibility occurring after an infectious disease, followed by a recurrence of the disease.

CASE II. This child, a five-year-old girl, whose family history is negative, was three years old before it was discovered that she had tuberculosis of the left knee. X-ray findings showed a mild lesion in the epiphysis of the femur, with some erosion of the posterior surface of the patella. After wearing a cast for two years, tuberculin treatment was instituted and continued without interruption until a dose of 0.80 c.c. of the first dilution of BE was reached in August, 1915. There was at this time a complete functional cure. The child seemed in perfect health and was discharged as cured by the physician who had administered the tuberculin according to the technic outlined in this work. On account of the seemingly good result obtained, the doctor did not urge upon the parents the continuation of the treatment, nor were they instructed to bring the child for the trimonthly tests. Six months after the last dose of tuberculin the child took sick with measles. Two or three weeks later she began to complain of pain in the knee, with limitation of motion, and there was a temperature (rectal) rise to 101° F. daily. In this case, treatment was resumed with the third dilution.

FIG. 40

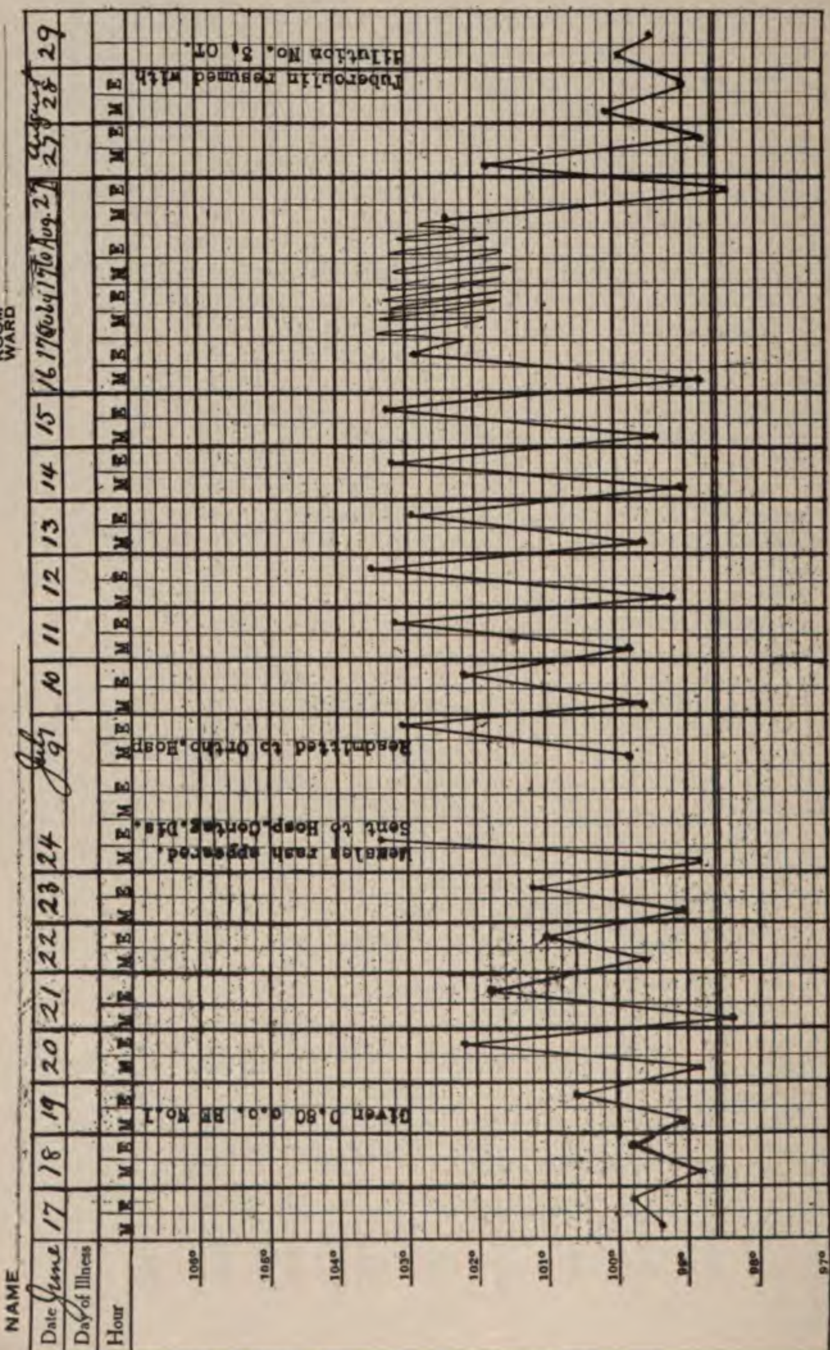


Since the temperature did not rise until the third day and there was no local reaction, the rise was thought due to a cold, and when the temperature dropped to 100.2 F. on the day for reinoculation, the dose was increased in the usual way.

After two weeks of normal temperature tuberculin treatment was resumed allowing for increased hypersusceptibility due to the measles.

The dose was increased by 0.10 c. c. in order to more quickly reach the maximum tolerance in case dilution No. 3 was too great a reduction in dose. The reaction indicates how nearly right we were in beginning with dilution No. 3. After an interval of one week, treatment was resumed with 0.10 c. c. of No. 3 and continued as per Table I, page 57.

FIG. 41



Temperature rise considered a constitutional reaction until rash appeared.

The high temperatures which were brought about by the measles remained high for seven weeks. The tubercular process which was nearly healed became active. After the temperature became normal tuberculin treatment was resumed with the dose reduced to 0.10 c.c. of dilution No. 3.

Part III

SPECIAL TREATMENT

Chapter I

INTRODUCTION

Up to the present day, most of the work done with tuberculin has been done by lung specialists, and in sanatoriums where the hygienic dietetic treatment, and all other adjuncts of tuberculin treatment have been followed out as a matter of course. However, in the teaching of tuberculin treatment the importance of these measures as an adjunct to tuberculin has been overlooked, resulting in their neglect when tuberculin was given a trial.

Tuberculin should not be employed to the exclusion of other therapeutic measures.

Since this work is calculated to emphasize the value of tuberculin in surgical tuberculosis, the use of tuberculin would be doomed to failure, in the large majority of cases, were we to neglect the other measures which are just as vital in bringing about a cure. We must bear in mind that tuberculin can overcome only the infection; that the disease, which in surgical cases has persisted for years, has left its traces behind in the form of pathological changes; and that unless we apply correct measures to these at the same time, we cannot hope to produce appreciable results.

The action of tuberculin is specific against tubercular infection, and not against the attendant processes which occur as a result of the tubercular infection.

To the patient, it is just the same whether his fistulas or bone cavities are kept open with a discharge of pus due to the streptococcus or staphylococcus, or whether the discharge is due to the tubercle bacillus. While from a medical standpoint, the elimination of hypersusceptibility with tuberculin is already of great advantage to the patient—by checking, as it does, the further spread of the tubercular process—still, the local manifestations of mixed infections are just as troublesome and tend as much to invalidism as before.

The consequent processes may continue the invalidism after the disappearance of the tubercular process.

The application of orthopedics is necessary to bring about good results from tuberculin therapy.

Again, tuberculin must not be understood to take the place of orthopedic treatment, for the deformity is not caused by the tubercular infection itself, but by the results of the tubercular process. In arresting the infection with tuberculin we do not correct deformities and do not replace destroyed joints or bones.

At the same time, although the aim of orthopedic treatment is to prevent or correct deformity, it cannot claim to stop the infection. And all orthopedic appliances can be of no avail, unless during their application, a natural resistance overcomes the infection. Otherwise, in spite of the appliances, even under the best of circumstances, the recurrence of these deformities may take place.

Tuberculin therapy will act as a guide to the application of orthopedic treatment.

However, the combination of orthopedic and tuberculin therapy is ideal: the immunotherapy to limit the disease and to overcome susceptibility, the ortho-therapy to prevent deformity. The tuberculin will, moreover, act as a guide to the limitation of orthopedic treatment—it will be unnecessary to order the cumbersome appliances to be worn year after year, for tuberculin will do away with the element of "guess," which has to be so prominent in orthopedics. For with the conviction of having checked the infection and overcome the susceptibility, the length of time for orthopedic application can be gauged more accurately.

Surgical interference must be limited to the conditions outside of the influence of tuberculin.

The same holds true of the application of surgery in tuberculosis. Eliminating the danger of extension of the disease by overcoming the susceptibility to tuberculosis before surgical interference, will not only reduce to a minimum the amount of surgery required, but that which is required can be done with greater safety.

Cicatrized tubercular glands may be removed under local anesthesia, with the most conservative incision, whereas tubercular glands removed without a previous tuberculin treatment very frequently recur even after a radical operation.

Whether tuberculin treatment is necessary to make other

methods of treatment efficient, or whether other methods are needed to make the tuberculin a success, the fact remains that a combination of certain methods of treatment is vastly superior to each one alone.

Tuberculosis is a combination of processes, hence—a combined therapy is most rational.

We have also advocates of bismuth paste in tubercular cavities and abscesses. There is no doubt that in isolated cases we have good results from the use of bismuth paste alone. And since we cannot differentiate between the cases which should have bismuth alone, and which should have tuberculin alone, why not avoid failure from a wrong choice by using both in all cases? There is no doubt that the bismuth acts purely mechanically by establishing a high specific gravity in the cavity or fistula. It thus prevents negative pressure, which is the cause of exudation of serum and lymph, the accumulation of which forms the best culture medium for the further growth of bacteria and thus continues the pathological process indefinitely. So by the use of bismuth paste we overcome a prominent factor that continues the subjective symptoms of the disease which is beyond the province of the mechanism of immunity.

As regards the application of hyperemia, the tuberculin therapy is again of inestimable value. Bier reports excellent results with hyperemia alone, and since the part of the mechanism of the immune response is a focal reaction consisting of hyperemia, the introduction of Bier's hyperemia may be of great value during the course of tuberculin treatment. In fact, in isolated cases, it may provide the elements of success in an otherwise stubborn case. There might have been some obstruction to circulation, or some other element which may have prevented focal reaction; or the antibodies may not have been able to reach the point of infection; but with the addition of the artificially induced hyperemia, we were able to bring the immune elements to the point of the local infection.

Since we are dealing here with the natural forces that are instrumental in overcoming infection, and the assistance

The necessary, immediate surgical measures may be greatly modified in the presence of increasing immunity acquired during tuberculin and vaccine treatment.

we give consists in intensifying these processes, the usual surgical measures that are deemed necessary can be more or less modified, not only as to the time of operations as suggested above, but also to the extent of these surgical measures. Thus, if the increased supply of antibodies will overcome the bacterial invasion, it stands to reason that the evacuation of the pus already present is quite sufficient without the establishment of drainage. For the same reason, wide incisions may be dispensed with, and either aspiration or puncture may suffice. At any rate, the increased immune response will eliminate the danger of the spread of the infection even though it may not be quite enough to prevent the local formation of inflammatory products. In this case, the puncture will be sufficient to prevent such discharges from being retained; and the trouble of re-aspiration will be more than repaid by the final cosmetic effect.

The cold abscess requires greater attention than has been accorded to it.

In this connection, it is also well to remember that the pointing of cold abscesses may not be due to mixed infection at all, but to a digested ferment which is excreted by the cells lining the abscess. These ferments digest the tissues of the wall, enlarging the abscess in all directions, giving it the appearance of pointing when the process approaches the surface. Puncture or aspiration is absolutely essential under these circumstances before the process has come too near the surface; for unlike an infection, there is no inflammatory hyperemia surrounding the area where the abscess breaks through. Hence, the unresisting surface forms more or less a sloughing process, causing a very ugly broken-down surface with ultimate extensive scarring.

Chapter II

MIXED INFECTION

Too little attention is given to co-existing infections in tubercular processes.

The subject of mixed infection is recently receiving more attention than it has been getting for some time. However, it still falls far short of the attention that it deserves. One cannot work in tubercular conditions very long without becoming convinced that many a patient would have succeeded in overcoming the tubercular infection were it not for a mixed infection that kept the flame smoldering.

The removal of the mixed infection will clearly define the extent of the tubercular process, and thus simplify the tuberculin treatment.

One need not be surprised in coming here and there upon a case where a vaccine for a mixed infection will clear the whole trouble. The balance between the infection with the tubercle bacillus and the mixed infection with the other bacteria is sometimes so fine that it is difficult to determine which is producing the symptoms. This is particularly true in patients running a temperature. We can avoid wasting a great deal of time during the tuberculin treatment when a temperature is caused by mixed infection; for if we consider that temperature of tubercular origin, the amount of tuberculin we are advised to give will be far less than for a similar condition without temperature. Now, if we can clear the temperature by means of a mixed infection vaccine, the tuberculin treatment in such cases will then be more definite and accompanied by less hesitancy as to its continuation.

The empirical application of vaccines has hindered their wider use.

Perhaps a great deal of hesitation in the use of vaccines in mixed infections is due to the indefinite results often obtained with them. These faulty results are another illustration of the ineffectiveness of the stereotyped use of a therapeutic agent that depends upon the stimulation of natural processes which are so complicated and so different in different individuals. We cannot administer vaccines any more than tuberculins in formulated recipes, as we admin-

ister drugs. Nor can we use vaccines without absolute definite reference to the causative bacteria, to the virulence of the infection, and to the individual resistance.

Diagnosis of Infective Organism

A correct diagnosis of the causative organism is essential before a proper vaccine can be obtained for the treatment of a mixed infection.

A momentary contemplation of the heading of this topic will impress the reader at once with the importance of this subject. Nevertheless, very little has been said on this subject in the past, and still less has been done. It is therefore clear that the element which would have rendered the whole subject of vaccine therapy much simpler and infinitely more scientific has been entirely overlooked, namely,—the bacteriological diagnosis of the infection. Some have depended upon the laboratories to make their vaccines and to give the directions for their use; while others have used mixed vaccines which were supposed to be applicable for all forms of infection. Again, proprietary mixtures were employed with a list of diseases for which they should be used, and with directions for dosage. As neither the laboratory nor the proprietary manufacturers can have any idea of the condition in question, the physician administering the vaccines not only fails to understand the composition of the vaccines, but is just as hazy with regard to the infection with which he is dealing.

All this forms a condition in the sphere of immotherapy that may lead not only to bad results but even to a premature death of the entire subject. Such a state of affairs would bring about no less a calamity than the loss of the value of tuberculin in tubercular conditions.

How different would the aspect of vaccine therapy be if due consideration would be given to the diagnosis of the infection? Once the diagnosis of the infectious organism is established, we could then demand from the laboratory a vaccine made from the infectious organism no matter what other bacteria happened to contaminate our culture media or our infected material.

Or if the stock vaccine be used, we could simply purchase a vaccine for this particular infectious organism. We could then treat the patient with the specific vaccine, and abandon the use of a mixture of organisms which we have been using with the hope that one of them may reach the mark the rest having no bearing on the infection. Having made the diagnosis, the appropriate vaccine will be an agent of precision in the hands of the physician, and will do away with probing in the dark which is brought about by an insufficient knowledge of what is being accomplished during treatment.

It will be possible to gauge the treatment by the condition at hand, and acquire that exactness which alone will make possible the clear insight into the mechanism of immunotherapy.

To arrive at an exact diagnosis of the infection, we have the following methods at our command: the smear for microscopic examinations; cultures on appropriate culture media; physical diagnosis; and animal inoculation.

Smear Diagnosis. It is not necessary to have a special biological training in order to be able to utilize this form of diagnosis. The variety of bacteria that we deal with in the more common infections and especially in mixed infections in tubercular patients are few in number and easily distinguishable. A few hours of reading in any of the simpler text-books on the subject will be sufficient to give all the data that are necessary for a working basis in vaccine therapy.

A simple smear stained with methylene blue, will disclose under the microscope the causative organism in the large majority of instances.

In the majority of cases, the simple methylene blue stain will suffice. In others, a differential stain for the tubercle bacillus and perhaps Gram's stain may be used. All in all, the making of a smear diagnosis of mixed infection consists in making on a slide a smear of the pus discharged from a fistula, or sputum; fixing it in the flame; then covering it with an aqueous solution of methylene blue for a minute or two; rinsing the slide; then when dry placing a drop of

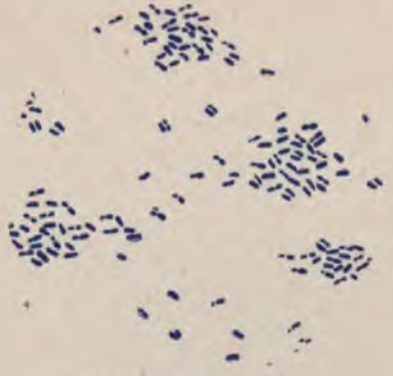
cedar oil on it; and finally examining it with the oil immersion lens.

The staphylococcus, the streptococcus, the colon bacillus and the pneumococcus are so easily distinguishable that one does not require a second glance in the microscope to recognize the offender. Of course, frequently secretions contain so few of the offending organisms that we must depend upon a cultural growth for diagnosis. (This subject will be discussed under the heading of "Cultures.")

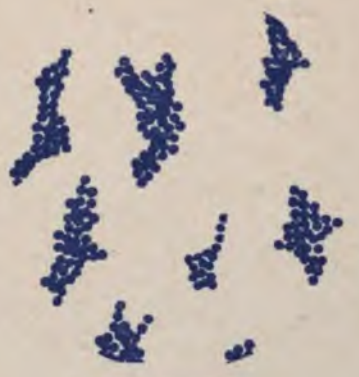
But a short practice with smear diagnosis is required to make it evident that very frequently the offending organism fails to grow in the culture tube even though it is evident in the smear. It is a known fact that the more virulent a bacteria, the greater the difficulty in obtaining a growth on an artificial medium; and that the avirulent strains not only grow more readily on the artificial medium but will inhibit the growth of the virulent bacteria which are necessary for the production of the vaccine. Thus it may happen, that the smear shows a streptococcus, while the growth in the culture tube reveals a staphylococcus, the latter having either gotten in through a surface infection, or from the pus where it took no part in the actual infection. This staphylococcus being avirulent, crowded out the streptococcus by its rapid growth. So long, however, as a smear revealed the streptococcus as the causative organism, a second or even a third culture will finally yield the proper growth for a vaccine. If a culture is sent to a laboratory, the request must accompany the culture to make the vaccine of the organism found to be the one causing the infection. The laboratory will find no difficulty in isolating the causative organism through subcultures, and if it fails to grow, the laboratory will so report to the physician and avoid making a vaccine of the wrong bacteria. This can be accomplished only by a correct diagnosis of the causative organism in the first place. A large number of failures in vaccine therapy will thus be eliminated. Moreover, the practice of smear diagnosis brings us

Fig. 42—Pyogenic Bacteria—Methylene Blue Stain

a—Streptococcus



b—Colon Bacillus



c—Staphylococcus

face to face with the enemy we are fighting, consequently simplifying the whole subject; and since simplicity leads to precision, the labor involved carries with it a commensurate compensation.

Cultures. One of the important points of consideration in the steps between the infection as it presents itself to us and the vaccine is the inoculated culture tube. The proper media are easily obtained and all that is necessary in order to get the proper vaccine is a growth of the bacteria that is causing the infection. The culture tubes are put up in convenient form for inoculation and transportation. However, if we are to utilize the appearance of cultural growth for diagnosis, we have to grow the bacteria in our office, and at the proper incubation temperature.

The appearance of the cultural growth may aid in the diagnosis of the causative organism.

Here again, a serious barrier to vaccine therapy seems to arise in the shape of costly and complicated apparatus. If we remember, however, that the essential for the growth of the bacteria is a temperature of 97° to 99° F., the means by which we can maintain such temperatures is of no consequence. Hence, it sometimes suffices to carry the culture tube in the inside vest pocket, if a culture is taken in the morning, in order to obtain a sufficient growth for diagnosis by the evening. Another convenient means of incubation is a thermos bottle. This may be filled with water at a temperature of 101° or 102° F. The infected culture tube when placed in water, will reduce the heat to about 98° F. Care must be taken to prevent the water from entering upon the culture media.

The cultural growth of these bacteria is required not only for the diagnosis of the invading organism, such as the differentiation between the albus, aureus and the citreus forms of the staphylococcus; but it is also necessary where the laboratory for the making of the autogenous vaccine is at a distance, requiring the transportation of the culture tube under adverse temperature conditions. Under these circumstances, the growing of these bacteria before trans-

portation or exposure will make it possible for these bacteria to reach the laboratory alive. We know the difficulty in growing the streptococcus; how quickly it dies under the best conditions in the culture media. An incubation at proper temperature for about twelve hours will so increase the number of these bacteria that a sufficient number of them will reach the laboratory for sub-culture and for the manufacture of the vaccine. Here again, as in the case of the smear diagnosis, an intimate knowledge of the physical appearance and of the characteristics of these few important organisms is essential—a knowledge that will not only bring about a gratifying understanding of the subject, but will help materially in the success of immunotherapy.

The diagnosis of the causative organism by means of animal inoculation is so seldom necessary that it requires no consideration here.

Animal Inoculation. Fortunately bacterial diagnosis does not frequently call for animal inoculation. When it does, it applies only to the tubercle bacillus.. Many cases where animal inoculations may be thought necessary can be cleared up by resorting to tuberculin tests as described under their respective headings in the chapter on "Tests."

Thus the field of animal inoculation is exceedingly limited. In those exceptional cases where this method remains the only source of diagnosis we must resort to it only if we are not within reach of a well-equipped laboratory. Otherwise, it may be found simpler in such instances to give a course of tuberculin even if it entails the eventuality of treating a non-tubercular case with tuberculin. No harm can be done with tuberculin in a non-tubercular case, whereas a great deal of good will be accomplished if the case is tubercular in nature.

The physical appearance of the pus and of the infected area may sometimes aid in the diagnosis of the causative organism.

Physical Signs. Occasionally we have to deal with an urgent form of mixed infection where it is necessary to use a stock vaccine immediately and where the infection is beyond reach, making a smear or culture impossible. In such cases we may sometimes get a fairly good clue to the nature of the invading organism by means of physical signs. Thus, the temperature curve may point to a streptococcus infection.

An erysipelas can be diagnosed from outward appearance and a stock erysipelas vaccine used. A septic condition with a sero discharge may point to a streptococcus infection; and a creamy discharge, to a staphylococcus. The odor of a discharge may point to the colon bacillus. The location may occasionally be a clue, as for instance, a mixed infection in kidney tuberculosis would point to a colon infection.

The following history illustrates the importance of the correct diagnosis of the causative organism.

The patient, a woman twenty-eight years of age, was operated on by suprapubic cystotomy for severe hemorrhage into the bladder from tuberculous ulcerations in the bladder wall. Three or four days later she had a severe chill, followed by temperature rise to 104° or 105°, and for ninety-three days this daily temperature rise continued, with remissions to below normal. Her condition at this time became very grave. She was greatly emaciated. About the ninetieth day, tubercle bacilli were found in her urine and for the first time the tuberculous origin of the trouble was discovered. This discovery was responsible for my being called in on the case by the attending physician, who knew my work with tuberculin. The question of vaccine had not been considered up to this time. As previously stated, acute infection had now lasted for ninety-three days, and on examination I found her suffering from what appeared to me to be a streptococcus septicemia. All urine came from the suprapubic incision, but was not recognizable as urine; it was a thick, creamy discharge having a microscopic appearance of pure pus and which on analysis showed urinary elements. A microscopical examination showed numerous tubercle bacilli, a short-chain small streptococcus, a staphylococcus, and a small micrococcus, the identification of which we did not deem worth while at the time. Suitable culture media were at once inoculated and a vaccine of the streptococcus was ordered. Meantime a stock streptococcus from a similar condition was at once administered in order not to lose time in waiting for the autogenous vaccine. Repeated laboratory reports, after cultures on various media, stated that no streptococcus grew in the media, and not until almost a week had elapsed did the streptococcus finally grow. Until then the growth always showed a small micrococcus unidentified, a staphylococcus, or the colon bacillus; but these were rejected as I was convinced from the pus appearance in the smear, and from the course of the infection that the streptococcus was the causative organism. The stock vaccine proved efficient; not only had the patient's temperature dropped to normal within forty-eight hours after the first inoculation, but after three more inoculations, during a period of two weeks, she was out of bed. Pure urine appeared from the suprapubic wound with only a microscopic trace of pus. Tuberculin treatment was instituted ten days after the first inoculation of vaccine. During the following four months of treatment, the suprapubic wound closed completely; the urine became free from tubercle bacilli; and the patient's weight which had been ninety pounds increased to one hundred and sixteen pounds.

Incidentally this case demonstrates the successful treatment of renal tuberculosis with tuberculin. It is now a year since the conclusion of treatment, and none of the symptoms referable to renal tuberculosis or bladder ulcerations have reappeared.

Chapter III.

VACCINES

Definition.

It does not come within the scope of this work to give a detailed account of the methods of preparing vaccines. I shall enter into it more in detail in a forthcoming work dealing with vaccines exclusively. However, I might mention that a vaccine is a watery suspension of dead bacteria, the bacteria killed in such a way as to produce the least morphological or chemical change in the bacteria. Such alteration must be avoided in order that the bacteria retain their power of stimulating the specific antibody when inoculated.

Preparation

In the preparation of vaccines a sufficient quantity to complete the treatment should be made.

It is necessary to make sub-cultures from the original inoculated media, in order to make sure that we have a pure culture of the specific bacteria. A sufficient growth on the sub-culture must be obtained in order to get a sufficient quantity of vaccine for the entire treatment. For after vaccine treatment has been instituted, it may become impossible to obtain growths from the discharges even though complete immunity has not yet been established. This would necessitate waiting for a recurrence of the infection in order to be able to obtain more vaccine,—thus causing unnecessary delay and vitiating to a large extent the former vaccine treatment.

Standardization. The standardization of vaccines must be made as nearly accurate as possible. I have seen a great deal of harm done by faulty methods of standardization.

Proper standardization is essential.

The following example may serve to bring out the necessity for proper standardization more effectively than any discourse I can give on the subject.

A comminuted fracture of the elbow joint became infected, and showed the staphylococcus albus in pure culture

as the causative organism. A vaccine was made, and standardized by a method of comparison of the viscosity of the vaccine with test tubes filled with known strengths of vaccines. The first dose administered produced a violent negative phase. The violent rise of temperature and tremendous increase of the local inflammation was not attributed to the vaccine, but to the extension of the infection. I was summoned in consultation; and from the appearance of the temperature curve, I was convinced that it was due to a negative phase. The undue turbidity of the vaccine led me to bring it to our laboratory for re-standardization. The bacterial count disclosed the vaccine to be nearly one and one-half times as strong as the label read. The infection cleared up after two injections of the vaccine, doses being used according to the new standardization. The effect was so marked that it left no room for doubt that it was brought about by the proper use of the vaccine. Example.

The best methods of standardization of bacterial suspensions in use at the present time are:

1. Wright's Method, which requires the mixing of equal parts of freshly drawn blood from a healthy individual (usually from the worker's own finger), and bacterial suspension diluted and stained, and placed in a counting chamber, in the same manner as for red blood count. The number of bacteria and the number of red blood corpuscles are counted in a number of squares, and an average is obtained for each. By figuring the proportion between the bacteria and the red blood corpuscles to the known five million red blood corpuscles per cubic millimeter, the number of bacteria per cubic millimeter will be obtained. This number multiplied by ten will equal the number of bacteria per cubic centimeter.

2. By a direct count of the number of bacteria, in the same manner and by means of the same apparatus as a blood count for the number of red corpuscles is made.

For more specific directions, see any laboratory guide.

Improper containers will frequently produce negative results from vaccine treatment of mixed infection.

Containers. At first glance, it may seem trivial to even mention the subject of containers for vaccines. But the success of vaccine therapy may sometimes depend on a minute detail.

For one thing, the former method of dispensing vaccines in ampules should be discarded. The sealing of the ampules necessitates the drawing out of the heated glass to a very thin neck. If, perchance, the box containing the ampules is allowed to stand for a day or two in such a position that the ampules are upside down within the box, the bacteria will precipitate into the very thin neck. When the vaccines are administered, these thin necks are filed or broken off and thrown away with the active principles of the vaccines. Even though we recognize the precipitated bacteria in the neck, and attempt to shake it out into the body of the ampule, we may in many instances only half succeed and so make our administered dose quite different from our intended one.

The following case will not only illustrate the necessity for good containers, but will emphasize the fact that attention to details is absolutely necessary when dealing with immunotherapy:

Example.

A girl, twelve years old, was sent to me for advice as to the use of vaccine for a colon pyelitis. One year previously she had a kidney removed for the relief of a severe pyelonephritis. Since this was an infection of her only kidney, surgical intervention was out of the question this time,—this fact forming the main reason for referring the case to me. I advised the use of vaccine, and gave full directions as to dosage, etc.

Three months later the little patient was brought to me by the mother, upon the advice of the physician in charge, with the statement that the vaccines had produced no result whatever. The temperature records showed that the daily rise between 101° and 102° F. previous to the vaccine treatment, had in no way changed during the treatment. Urine exami-

FIG. 43

FIGS. 43 and 44 show a good form of container—an ordinary bottle holding 18 c.c. The rubber cap fits tightly over the mouth of the bottle rendering it air tight. The cap is of good quality rubber, remaining air tight after puncture with the needle. When obtaining a dose of vaccine for treatment, the needle is first plunged through the cap in order to admit air to overcome the vacuum created by the previous withdrawal of vaccine, Fig. 43. The bottle is then turned upside down, the syringe connected to the needle, and the required amount of vaccine drawn, Fig. 44. The needle is pulled out of the rubber cap without disconnecting it from the syringe, and the vaccine is ready to be administered.

FIG. 44

nation showed just as much pus and bacteria as ever. Since vaccine therapy in this case was considered a method of last resort, the child was now again referred to me with the hope that personally I might be more successful than through the physician in charge.

The patient's mother brought with her the autogenous vaccine which consisted of a box of ampules, each ampule containing one cubic centimeter of the vaccine. This vaccine was made at the Polyclinic laboratory and there was no question as to its proper standardization. I took one ampule and noticed the precipitate in the neck. I began to shake it very vigorously, and continued to shake it for some time until all visible precipitate was out, and the clear fluid in the body of the ampule became viscid. I then broke the neck off and drew the appropriate amount into the syringe ready for inoculation. My vigorous efforts at shaking the ampule attracted the attention of the little girl, who thereupon exclaimed to the mother, "Doctor ——— never did that. Has something happened to the vaccine on the way over?" The reason for the failure of at least eighteen inoculations of vaccine given previous to this consultation at once became evident. The child had been inoculated with normal saline plus one-half per cent. phenol, but with no vaccine. That went into the waste with the discarded neck of the ampule.

After two inoculations at my office the temperature was normal and after four more all traces of pus disappeared from the urine. The child gained rapidly in weight, increasing in the next thirteen months at least forty per cent. over her former weight.

The best container consists of a bottle holding between five and twenty cubic centimeters, covered with a good quality rubber cap through which the needle may be plunged and the appropriate amount aspirated. (Figs. 43 and 44.) Little bottles containing one cubic centimeter each and corked with a minute rubber cork, will frequently modify

Proper care of vaccines.

the active principle of the vaccine. I have seen the precipitated bacteria cling to the cork when pulled out, even after vigorous shaking, if the box containing the bottle had been placed upside down for a length of time.

Care of Vaccines. Vaccines should be kept in a dark place. They should be kept in a cool temperature,—preferably in an icebox. They are never to be used when the color changes and the liquid begins to assume a brownish hue.

Stock Vaccines

An autogenous vaccine becomes a stock vaccine when used for a similar infection in a different individual.

A stock vaccine is a vaccine that is derived from an organism not taken from the lesion to be treated. The general notion of a stock vaccine is that it is manufactured and put up for commercial sale by some concern dealing in biological products. This conception entirely overlooks the fact that any autogenous vaccine is a stock vaccine when used on another individual suffering from an infection caused by the same bacteria.

Such a stock vaccine coming as it does from an infection which we have handled, can be labeled with a short description of the case it was derived from. These descriptions can serve to subdivide our vaccines of the same organism into various forms of infections caused by the same organism. Thus we are able not only to have stock vaccines of certain bacteria, but even in a general way to obtain stock vaccines of different strains of the same bacteria. In that way, we can utilize our left-over autogenous vaccines as excellent stock vaccines for similar conditions. Whether stock vaccines are the left-over autogenous vaccines from other patients, or those sold on the market by proprietary concerns, there can be no doubt about their therapeutic value.

In the manufacture of a stock vaccine, the more the culture obtained resembles the strain of the causative organism, the oftener it will prove effective.

It is difficult to compare with accuracy the relative value of stock and autogenous vaccines. But a stock vaccine is effective in a sufficiently large percentage of cases to justify its use before an autogenous one is made.

However, there is one element in the consideration of

stock vaccines which has done much to discredit their use, and which we must eliminate before stock vaccines will merit recommendation. I am referring to the poly-vaccines put up for the market. The practice of poly-pharmacy, except in a very moderate degree is at all times to be condemned. But to apply the same principle in the matter of vaccines is indefensible. If we deal with an infection which is caused by more than one organism, a separate vaccine should be made of each, and administered in such proportions as the exigencies of the case may require.

The use of poly-vaccines has done much to discredit the value of vaccines in general.

Immunotherapy depends for its success upon a fair judgment of the immune response; and how are we ever to learn to estimate the effect of vaccine therapy, if we are to use a multitude of different bacteria with the hope that one of them will produce the desired effect. I have gone into great detail on the subject of bacterial diagnosis because of the importance of knowing the enemy with whom we are dealing. For a thorough understanding of our enemy is the first esential in effecting his conquest.

Why, then, grope in the dark with the use of vaccines? If, for instance, we are dealing with a staphylococcus infection, why use a colon or a streptococcus with it? Again, supposing that we have with a staphylococcus a colon infection; by the use of a poly-vaccine consisting of staphylococcus and colon mixed, the colon responds so much more easily to vaccine treatment, that a radical increase in its dose would be not only useless, but even harmful; and still, such radical increase will have to be made along with the necessary increase in the staphylococcus.

I heartily recommend stock vaccine; and the polyvalent product as put out by the better known manufacturers is excellent. But these vaccines should be sold only in separate containers of sufficiently high concentration to make it unnecessary to give a bulky inoculation when mixing two or more bacteria in case of multiple infection.

Polyvalent stock vaccines are to be recommended only when put up in separate containers.

It is for the physician to judge when to mix the vaccines

The mixing of the various bacterial vaccines in the treatment of a multiple infection should be done by the physician alone, as he is the only judge of the dosage required.

and the quantity that should be used of each. Happily, the proprietary concerns are now putting out vaccines of individual bacteria and of high concentration; so that the physician can have a container full of from ten to twenty cubic centimeters of each bacteria on hand. And after a careful diagnosis of the causative organism or organisms, he can draw into his syringe the proper quantity from each container as the case may require, and inoculate his patient with the mixture. In that way he will know what he is using. Subsequent smears, cultures or laboratory examinations will guide him as to the continuation or the elimination of any one of the bacteria that he has been using in the treatment of the infection. At the same time, he will not be treating the patient with a vaccine of all the bacteria at once, but will have the choice of administering a vaccine of one bacteria after another, a practice which will be found especially valuable and illuminating in mixed infections in tubercular subjects. The treatment of a tubercular condition offers a sufficient length of time for such practice.

Not only will the serial use often remove the necessity of using a vaccine for other bacteria besides the principal one he has chosen to begin with (the discovery will often be made, that the other bacteria merely kept company in a fungoid form), but it will also afford an opportunity for an experience in vaccine therapy that will more than repay for the trouble.

Autogenous Vaccines

The advantages of autogenous vaccine over stock vaccine: are:
1 It is always of the same strain of bacteria as the infection.
2 It is always fresh.

An autogenous vaccine is a vaccine made of bacteria grown from a culture taken from the infection that is to be treated. An autogenous vaccine has the advantage over a stock vaccine by being perfectly fresh. And an autogenous vaccine is not only a vaccine of the causative organism, but of the particular strain of that organism that is causing the infection. Bacteria, like all living things, are influenced by environment as to their finer physical manifestations, no two individuals are exactly alike, no two infections are ever

exactly alike even though caused by the same organism. Since the influences upon the growth and physical conditions of the bacterial organisms differ, the same bacteria from lesions in different individuals must differ in some respect or other. The result is a variety of strains in each form of bacteria. Probably this minute difference is of no consequence as far as the specific mechanism of defense which they stimulate is concerned. However, this minute difference may be cumulative and in the process of evolution a later strain may slowly acquire such different characteristics that it will exert a specific influence upon the defensive mechanism.

And it is under such circumstances that a stock vaccine, although of the bacteria in demand, may differ essentially from the causative organism in its antibody stimulation. Even a polyvalent vaccine, although composed of many strains of the same bacteria, may altogether have missed the particular strain required, or may contain so few bacteria of this particular strain, that it is not sufficient to produce the desired effect.

Especially in the case of streptococcus is it necessary to have the vaccine of the same strain as the bacteria causing the infection.

The variation in strains is best illustrated in the streptococcus which offers an opportunity to see the varied outward manifestations of the infection it produces, although the temperature curve and the general constitutional effects may be similar. Thus it may produce a streptococcus septicemia, or an erysipelas; at another time we may have an acute arthritis, scarlatina, etc. These strains of the streptococcus may vary so distinctly that we have given them different names according to their physical manifestations, as for instance: the streptococcus viridens, streptococcus hemoliticus, streptococcus erysipelas, streptococcus ficalis, etc.

At the present time, we can obtain stock for any one of these particular strains; but to make a diagnosis of the strain at hand, in order to be able to specify the stock we are to use, we must in many instances employ the help of a laboratory. It might therefore be wiser to utilize the laboratory

for the making of the autogenous vaccine since the main reason for the employment of the stock is the fact that a great many physicians, especially in the small towns, have no laboratory within convenient reach. The expense item is no longer to be taken into consideration since the cost of making autogenous vaccines has greatly diminished in the last few years, and many State laboratories are furnishing them free.

Of course, haste must not be an excuse for choosing stock vaccine; for where there is the necessity for haste, there is always the greater necessity for accuracy. We can, however, administer stock vaccine pending the making of the autogenous vaccine.

In the manufacture of bacterial vaccine,—stock or autogenous,—the less delay between taking the culture from the infection and the completion of the finished product, the more active the vaccine.

In ordering a vaccine, we must remember that in its manufacture the more the bacteria retain of their characteristics, both physical and morphological, the greater the therapeutic value of the vaccine. It is therefore necessary to place the inoculated culture tube at body temperature as soon after inoculation as possible in order to enable the making of the subcultures twenty-four hours later. Longer growth of the original culture may modify the causative organism by too long a contact with the products of metabolism of the other organisms which might be growing in the same culture tube through accidental contamination.

The more concentrated the vaccine, the smaller is the bulk to be inoculated.

In making subcultures, we must remember that the more concentrated the vaccine, the smaller the bulk for each inoculation. Thus sufficient subcultures should be made in order to make sure that there is sufficient growth for a high concentration without the necessity for longer growth than twenty-four hours. In short, the less time that intervenes between the original inoculation of the culture tube and the completion of the vaccine, the better the vaccine will be.

Chapter IV

TREATMENT OF MIXED INFECTIONS

Classification: 1 Acute Infections: a. febrile; b. afebrile. 2 Chronic Infections.

It is best to consider mixed infection apart from the tubercular process when dealing with the use of vaccines in its treatment, and in so doing classify the infections into two distinct groups: the acute and the chronic. The sub-acute group need not be separately considered when dealing with infection in relation to immunotherapy, for the treatment is the same for the sub-acute as it is for the chronic. However, the acute form is best subdivided into two groups: the febrile and the afebrile.

Mixed respiratory infections have to be considered under a special topic (Part III, Chapter V) as their treatment differs somewhat from the treatment of surgical infections.

Acute Mixed Infections

Acute Febrile Mixed Infections. From the nature of things as they hold true in acute febrile infections, one would assume that vaccine would be useless in such conditions. This being essentially a treatise on tuberculin treatment, we cannot go into the theories and detailed descriptions of conditions existing in febrile affections to refute the frequent assumption that vaccines are useless and even dangerous in these conditions. But for the purpose of avoiding unintelligible gaps in this important subject, I shall simply add the following remarks to what has already been said in the theoretical part of this book:

Vaccines do not add toxicity to the individual.

Vaccine in the quantity administered for the purpose of treatment is not toxic, hence we *do not* "add toxins to the body which is already saturated with toxins." Vaccines merely stimulate antibody formation at the site of inoculation even in the presence of a general infection. And although fever indicates a maximum amount of resistance,

forming a condition unfavorable to bacterial growth,—it is true, nevertheless, that we have periods of lowered temperature between the heights of the curve, representing periods of exhaustion. The period of exhaustion forms a condition entirely favorable to bacterial growth, during which the antibodies coming from a new source can do much to hold the infection in check.

Vaccines stimulate the formation of antibodies.

Thus if we will consider the administration of vaccine in febrile infection as an aid to the natural protective mechanism, and if we mean to bring that aid when it is needed,—in other words, if we are to gauge the administration of vaccine so that its maximum effect will come during the periods of depression, we shall succeed in holding the enemy in check during the exhaustion period.

The relation of vaccine administration to temperature curve.

To be more exact,—the vaccine should be administered about an hour or two after the height of the temperature curve for the day has been reached. Thus it has the greater part of twenty-four hours to exert its influence before the next temperature peak is reached. The immune response usually occurs within six to twelve hours after an inoculation. A supply of antibodies will thus be provided during a period in the temperature cycle when the patient's own resistance is at the lowest point.

The influence of the vaccine will then be noticeable on the following day's temperature cycle. A minimum amount of time, therefore, need elapse before we shall know whether this dose and the following dose of vaccine was effective or not, for if the dose happened to be insufficient, there will be no reduction in the temperature peak the following day, and a second inoculation should be given an hour or two after the height of temperature has been reached.

The temperature curve is a guide to the intervals.

What is true with regard to the time of administration is also true of the intervals between inoculations. The intervals have to be properly gauged to get the best results. Here again, by means of the temperature curve, we are able to judge the intervals most accurately. Once a temperature

curve has been reduced by vaccine, we are able to wait for the next dose until the temperature begins to show, by a tendency to recur, that the effect of the previous dose is wearing off. From here on, the intervals between the inoculations should be equal to the length of time between the one injection and the day before the recurrence of temperature took place.

DOSAGE

Bacteria	Beginning Dose	Amount of Increase
Streptococcus	25 million	10 million
Staphylococcus Albus, Aureus, Citreus	100 million	25 to 50 million
Colon Bacillus	50 million	10 to 25 million
B. Pyocyaneus	100 million	25 million

Vaccines for single or multiple acute infections.

In acute febrile infections we do not often deal with more than one bacteria beside the tubercle bacillus. A simple vaccine will therefore suffice in the treatment of such an infection. However, if more than one organism is found to be the cause of the infection, it is better to have a separate vaccine for each. For example, if a streptococcus and a colon are found, the proper dose of each can be mixed in the syringe and administered in one injection.

Vaccine treatment in relation to tuberculin treatment in febrile acute infections.

It is best to treat the acute mixed infection and to ignore the tubercular process until the temperature has come down to normal. That holds true whether the infection is present before tuberculin has been administered, or whether it occurs during a course of tuberculin treatment. In the latter case, the interruption of the tuberculin treatment cannot materially affect the tubercular process, as acute febrile infections do not last long, especially when treated with vaccine.

Once the temperature has come down to normal, tuberculin administration may be resumed even though there still remains the indication for further vaccine treatment. We must, however, gauge our vaccine inoculations so that they fall at least twenty-four hours before tuberculin is adminis-

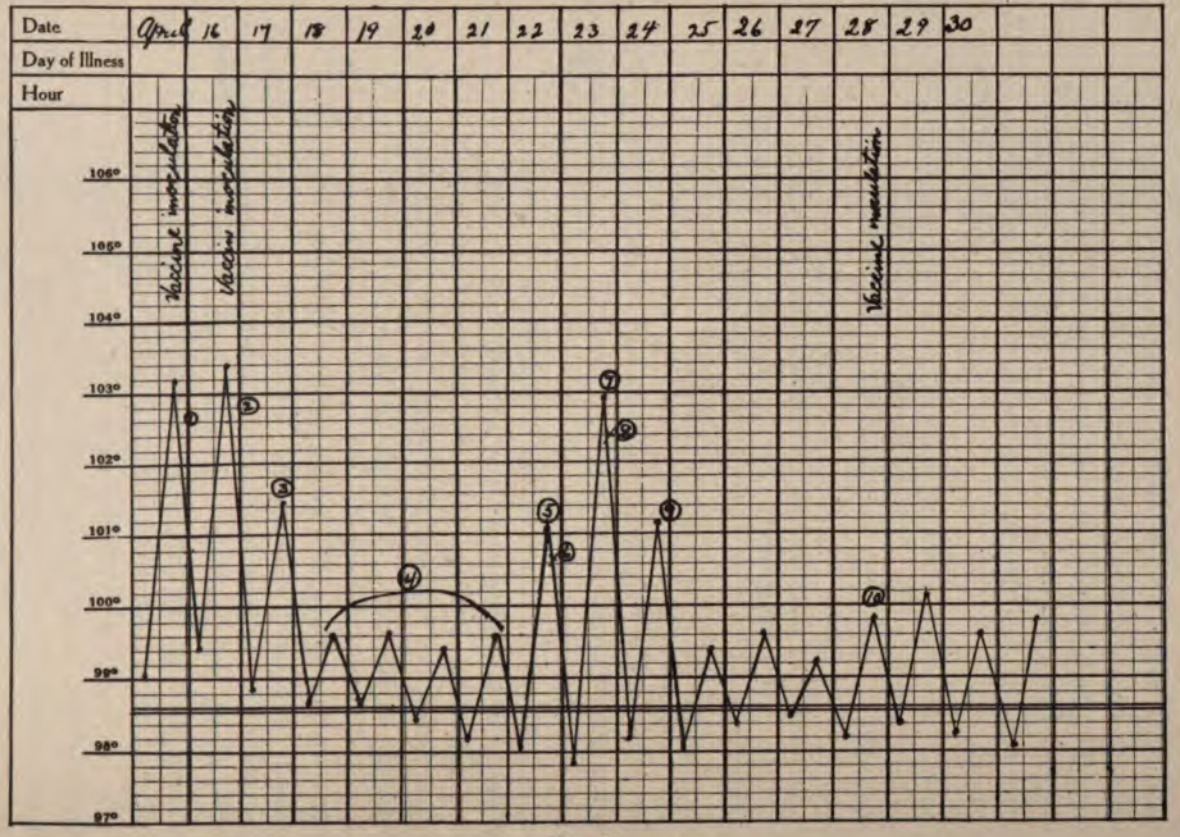


FIG. 45

(1) Vaccine inoculation soon after the peak of the temperature curve is reached, dose not effective. (2) Re-inoculation soon after the peak of the next day's temperature curve, dose effective. (3) The marked drop in temperature twenty-four hours after effective dose, the drop continuing to normal in forty-eight hours. (4) Period—vaccine remains effective. (5) The beginning re-rise of the next inoculation is withheld. (6) Time for the next inoculation to prevent the complete re-rise. (7) The complete re-rise, which takes place in forty-eight hours if next inoculation is further withheld. (8) Time of re-inoculation. (9) The amount of drop in twenty-four hours as a result of re-inoculation at (8). (10) The correct time for re-inoculation to prevent re-rise as determined at (4).

tered, or forty-eight hours after tuberculin was administered. The administration of vaccine at the same time or too near the tuberculin administration might interfere with the interpretation of the tuberculin reaction.

The correct differentiation between a mixed infection temperature and a tuberculin temperature is essential.

Before leaving the subject of acute febrile mixed infection, I must emphasize the importance of accurately differentiating between a febrile condition brought about by a sudden activation of the tubercular process, and a febrile condition brought about by a mixed infection. In an acute condition caused by the tubercle bacillus, the uselessness of a vaccine made from an avirulent organism is apparent. On the other hand, much harm can result from a failure to institute the proper vaccine treatment against an acute febrile infection occurring during a course of tuberculin treatment by attributing the temperature rise to an extension of the tubercular process, or to a tuberculin reaction.

Definition.

Acute Afebrile Mixed Infections. When an infection is acute, as evidenced by the acute local manifestations, and still produces no constitutional manifestations such as temperature with its accompanying symptoms, we have one of two conditions. Either there is an acute inflammation balanced by a high degree of resistance, with absorption of the inflammatory, bacterial, or cellular products, in quantities too small to cause constitutional symptoms; or else there exists a point of exit for the inflammatory products other than by means of the circulation. This exit may be drainage through an incision, or suppuration; or through sinuses or fistulas; or through natural channels, such as the ureter, urethra, bronchial tubes and so on. The following dosage has been found satisfactory in most instances:

DOSAGE

Bacteria		Beginning Dose	Amount of Increase
Streptococcus		50 million	10 to 20 million
Staphylococcus	Albus, Aureus, Citreus	150 million	25 to 50 million

Colon Bacillus	50 million	25 million
B. Pyocyaneus	100 million	25 million

Time and interval of vaccine administration in afebrile infections.

The time of administration is no factor in the treatment of afebrile conditions, as there are no periodic fluctuations between the infection and the patient's resistance. However, as regards intervals, a measure of accuracy must be applied. But not having the guidance of a temperature curve, we must be governed entirely by subjective or objective symptoms. Thus if there is no improvement in forty-eight hours, the patient should be reinoculated if the minimum dose was used in the first place. The intervals may be determined after improvement has taken place, by waiting with further treatment until a tendency for the recurrence of the symptoms appears. The vaccine treatment is then continued without again waiting for the recurrence of symptoms, but by administering the reinoculations one day before. The objective and subjective signs which act as guides for the determination of intervals and effects of the vaccine treatment in general are: pain, tenderness, swelling, redness, increased or diminished motion, the character and quantity of the inflammatory discharges, and so on.

Production of a negative phase should be avoided.

If a reaction occurs immediately after an inoculation, as evinced by increased symptoms (negative phase) the vaccine treatment should be discontinued until all signs of the reaction have disappeared. Usually, there is a period of improvement following such a reaction, which is more pronounced than the improvement following treatment, without the production of a negative phase. However, we should not purposely produce a negative phase for that would tend to the production of a permanent negative phase with its attendant dangers. The dose of vaccine following a transient negative phase should not be increased; however, it need not be diminished, as it is unusual for the same dose to produce a negative phase more than once. And when a negative phase does occur, it will be transient and therefore beneficial.

Conclusion of vaccine treatment

After the subsidence of the acute symptoms it is advisable to continue the vaccine treatment for a time, in order to maintain the immunity gained against the mixed infection. For this purpose it is sufficient to administer one dose of vaccine a week, continuing with slight increase for several weeks after all traces of infection have passed.

Stock or autogenous vaccines.

The element of time is frequently just as important in cases of afebrile conditions as it is in cases of febrile mixed infections. So that it may be advisable to use simultaneously a vaccine for each of the organisms found. However, in the majority of instances, it is practicable to use a vaccine for the preponderant organism first, and only then consider vaccines for the remaining organisms if the treatment with the first vaccine proved unsatisfactory.

Vaccine treatment in relation to tuberculin treatment in afebrile infections.

The tuberculin treatment can be continued without interruption during the vaccine treatment of acute afebrile mixed infections. However, if the mixed infection is of such an acute nature that rapid extension of the disease is threatened, and if shorter intervals than one week are indicated for the vaccine inoculations, one treatment a week with tuberculin would be sufficient until the mixed infection is under control.

The hyperemia of the tuberculin focal reaction is an aid to vaccine treatment.

The vaccine treatment of mixed infections in tubercular conditions has been observed to be more successful in tuberculin treated patients than in patients not treated with tuberculin. This may find explanation in the fact that tuberculin produces a hyperemia at the point of inoculation through the focal reaction, offering greater facility for the ready access of the artificially stimulated immune products, to the organisms causing the infection.

Chronic Mixed Infections

Definition.

Chronic infection from the standpoint of immunology is a state of equilibrium between the onslaught of the invading organism and the defense of the host. This equilibrium is maintained by means of various mechanisms. On the part of the bacteria, the failure to advance may be due to a loss

of virulence, or to an inability to penetrate the fibrous barrier which the host has built around the infection (incapsulation).

The formation of chronic infections.

On the part of the host, a failure to entirely overcome the invader may be due to an insufficient immune response; to a mechanical obstruction to circulation caused by a high coagulability of the serum carrying the defensive substances, thus clogging the tissue spaces and impeding the further arrival of antibodies; and to an insufficient carrier of the products of the immune response to the invading organism. The last is due to the occurrence of anemia instead of hyperemia at the point of infection. This anemia may be brought about either by a state of the blood, or by mechanical obstruction to the circulation at or near the point of infection in the form of a defensive capsule to stay the advance of the infection. Thus the very instrument of defense (defensive capsule) may become so formidable that connective tissue cannot penetrate through it. The formation of a permanent canal (sinus or fistula), or cavity, or both, takes place in which the invader can live and multiply in comparative security shielded from the immune bodies of the host.

This deadlock between infection and resistance may be maintained by a number of other causes which we need not discuss in further detail at this time. But it is necessary to have at least a cursory understanding of the elements of chronic infection in order to effect its final elimination.

Chronicity is most pronounced in bone tissues.

Nowhere is chronic infection *so chronic* as in tubercular bone diseases, for the tubercular process tends to form cavities in which the infective material gathers, causing the formation of fistulas through which the contents of the cavities are discharged.

Where the equilibrium between the resistance of the host and the virulence of the invader is the sole cause of chronic infection, vaccine alone is sufficient to cure such a condition. For with vaccine, we are able to add sufficient antibodies to those naturally formed to break the deadlock

in favor of the host, and at once accomplish a cure. But where other elements aside from the insufficient immune response are the cause of the chronic infection, such as fistulas and cavities and so on, we must look for appropriate methods besides vaccines to accomplish the final eradication of a chronic process. Such methods will be described under Bone Cavities, Sinuses and Fistulas.

The treatment of pathological changes brought about by chronicity must be considered apart from the treatment of the infection.

The dosage, as well as the increases, are somewhat higher in chronic conditions than in acute conditions.

DOSAGE

Bacteria	Beginning Dose	Amount of Increase
Streptococcus	100 million	25 million
Staphylococcus Albus	200 million	50 million
Staphylococcus Aureus		
Staphylococcus Citreus		
Colon Bacillus	100 million	25 to 50 million
B. Pyocyaneus	150 million	25 to 50 million

One treatment a week is most convenient and usually sufficient, but it must be so timed as not to interfere with the determinations of the bi-weekly inoculations of tuberculin.

A chronic infection in a tubercular subject constitutes a suitable condition for the study of the mode of action, and of the effects of vaccines. The character of the cases, and the length of time required for a course of tuberculin treatment offers a long enough period for any method of vaccine treatment we may find appropriate to apply. Thus I have found that in the long run the use of vaccine against one organism at a time in cases of multiple infection, not only produces better results but offers the best conditions in which to determine the exact rôle which each organism plays in mixed infection. For instance, if we have a streptococcus and a staphylococcus albus and a staphylococcus aureus in a mixed infection, by making an autogenous vaccine for the streptococcus or by using a stock streptococcus vaccine, we

Vaccines for single or multiple chronic infections.

can study by culture and by smear the effect of these vaccines on such infections.

If, after the streptococcus vaccine has been used for a reasonable length of time, and if the streptococcus disappears from the discharge without producing any appreciable effect either quantitatively or on its consistency, we can be reasonably sure that the staphylococcus aureus or the staphylococcus albus or both have been active in the formation of the infection, and will require the specific vaccines for their irradication. If, however, the discharge thins and becomes sterile after the use of the streptococcus vaccine, it is at once evident that the staphylococcus merely existed in the discharge in a parasitic form, or formed a coincident surface infection during the taking of the cultures while the real offender was the streptococcus alone.

By this method, besides saving time, expense, and trouble for the patient, we obtain a grasp upon vaccine therapy that no other method offers.

Of course, the necessity of working with cultures and smears may appear too complicated a task for the busy general practitioner. However, the whole matter may be made very simple and may even add another element of interest to his work.

The growing of cultures may be accomplished by the simple procedure described in Chapter II, Part III. Smears may be made on ordinary slides (which can be easily obtained) by first placing a drop of water on the slide; the material to be examined is stirred up in this drop of water and spread in a thin film, allowed to dry in the air, and fixed in the flame. The process of staining is still simpler. Loefler methylene blue is all that is required. A few drops are placed on the smear for one minute, then rinsed off with ordinary tap water, and after the slide dries the smear is ready for examination under the microscope.

To make matters still simpler, nature has endowed the pyogenic bacteria with very easily distinguishable features.

For example, the streptococcus is easily recognized by its chain formation; while the staphylococcus grows in groups. The albus, aureus, and citreus can be distinguished from their different appearances in the culture tube. The albus is white, the aureus a golden yellow, and the citreus a lemon yellow. And the colors are so distinct that there is no room for doubt as to their identity. (Chapter II, Part III.)

Chapter V

MIXED INFECTIONS IN PULMONARY TUBERCULOSIS

Mixed infection in respiratory tuberculosis consists of pyogenic and catarrhal processes.

Mixed infections in pulmonary tuberculosis differ so radically from mixed infections in other processes, both in their pathological forms and in their symptoms, that it is wise to go into a little more detail on the subject rather than to include it under the general heading of mixed infections. As was stated in the preceding chapter, a mixed infection merely means an infection with an organism, or organisms, superimposed upon and helping to continue the tubercular process. It rarely assumes an unusual form. In respiratory conditions, however, the mixed infection organism may not only exaggerate the usual symptoms of pulmonary tuberculosis, and animate the tubercular process, but may produce symptoms entirely apart from the tubercular process. Such infections may be sufficiently acute to be more dangerous to life than the tubercular process itself; they may upset all the beneficial results obtained with tuberculin, and render the condition hopeless.

Weather conditions and catarrhal processes in the upper air passages exert an adverse influence upon pulmonary tuberculosis.

Again, we must bear in mind what a tremendous influence weather conditions have upon a tubercular process in the lungs; for the intimacy that exists between the various parts of the respiratory system is self-evident. An acute rhinitis may alter the aspect of a tubercular lung condition, and a streptococcic sore throat may do for the pulmonary process what measles will do in any tubercular condition in the child.

The following three distinct situations for the use of vaccines exist:

In a condition of mixed infection in pulmonary tuberculosis it is not sufficient merely to make a vaccine of the offending organisms, but we must consider its application with reference to three distinct situations: First, the use of vaccine in co-existing mixed infections which add to the

chronicity of the process as they do in all other forms of tuberculosis: second, an acute or subacute infection co-existing with the tubercular process, interfering with or nullifying entirely the immune response to tuberculin; third, and most important, the use of vaccines in prophylactic immunization, during periods of the year when catarrhal inflammation, such as influenza, bronchitis, etc., are prevalent.

1. The pyogenic mixed infections; 2. Acute or subacute catarrhal infections; 3. Prophylactic immunization against prevalent infections.

It is ideal when dealing with so complex a problem as immunization in respiratory mixed infections to have the patient in bed under constant professional supervision, with a well equipped laboratory and trained laboratory assistants, to make daily observations as to the effect of the vaccines injected, and of the change in the organisms present. The percentage of physicians who have such facilities is so small that we cannot even dignify their number with the name of minority. Those who have these facilities, and are taking advantage of them, are rendering a great service by clearing many of the complexities connected with the subject, making it possible for us to utilize their experience to some extent in our practical application, however limited the field may yet be. For the vast majority of physicians who do not have these facilities, it is fortunate that we are easily able to find at least the most important organisms by simpler methods, and treat the patients with a fair measure of success.

For practical purposes only the most prominent bacteria need be considered for vaccine treatment.

Since this book is intended as a guide to the utilization of the immune response within the limitation of practical application, I shall avoid enlarging upon methods which can be carried out only by means of modern laboratory facilities.

The number and variety of bacteria that may be found in respiratory secretions is of necessity large because of the easy access that any bacteria has to any part of the respiratory tract. Not only are the canals open, but we directly invite the entrance of these organisms by inhalation, by the partaking of food, and by the deep recesses that can harbor bacteria and allow them to grow. Yet, not all bacteria found

in the respiratory tract, even during disease, are pathogenic; and when we have an infection in the respiratory tract it is very difficult to determine which of the organisms are at fault. However, some of them are commonly at fault.

In the treatment of respiratory infections existing in a tubercular individual, we must be content to make a vaccine of one or more of the easily recognized and easily cultivated bacteria that we find. Fortunately this will embrace a large enough class of cases to make it worthy of trial.

Even in the presence of a large variety of bacteria, treatment for the streptococcus, penumococcus, and the m. catarrhalis is sufficient in most cases.

The variety of organisms at fault is relatively small in cases of mixed infections in tubercular lungs. We find by experience that the streptococcus in a tubercular lung is most often concerned with the production of the added infection, whereas the staphylococcus is found to be the most frequent offender in infections in a non-tubercular lung. By using an autogenous vaccine of the streptococcus found in the sputum of a pulmonary tubercular patient, we very often clear the mixed infections to such an extent that it need not be reckoned with any further in the treatment of the tubercular condition. The staphylococcus is of course a frequent offender. The pneumococcus takes the third place. Less frequently do we have to deal with the micrococcus catarrhalis, the influenza bacillus, the Friedlander bacillus, and the micrococcus tetrogenus, except in prophylactic immunization during prevalent catarrhal infections. I have left other organisms out of consideration, because of the difficulty of isolation, and the frequency with which they disappear from the sputum after using the vaccines against the other organisms.

Chronic Respiratory Mixed Infections

Chronic respiratory mixed infections are of two varieties: 1. Infections superimposed

The chronic infections form the greatest majority of mixed infections in pulmonary tuberculosis, and in their consideration we must recognize two distinct types. The infection which implants itself upon a tubercular area as it does in bone and gland tuberculosis; and the catarrhal infec-

tion which prepares the soil for the tubercle bacillus. The former requires treatment only when we find that it aggravates the tubercular infection or interferes with the benefits derived from the tuberculin. The mere finding of bacteria in the sputum is not sufficient a reason to consider the use of vaccines necessary.

upon the tubercular process; a. Primary infections which created the traumatic condition, and which attracted the tubercle bacillus.

However, we have a more difficult problem to deal with in the treatment of primary mixed infections which resisted the process of natural immunity and treatment for a great many years, and which produced trauma in the lung, and attracted the tubercular infection in the lung in the same manner as direct trauma attracts the tubercle bacillus in a case of bone and joint disease. Here we must not lose sight of the various pathological changes that many years of catarrhal infection have brought about in the lung and bronchial tubes. These changes must be reckoned with in our expectations as to the results to be obtained from immunotherapy.

Mixed Infections Which Follow Upon a Tubercular Process. The number of bacteria that may implant themselves upon a tubercular process in the lung is very large and varied. The direct communication between the nose and mouth and lungs makes this possible. Fortunately not all the bacteria are pathogenic and not all of the pathogenic bacteria that find lodgment in the tubercular lung get beyond the saprophitic form. Even those that do become virulent and help in the pathological changes brought about by the tubercular process naturally become extinct during the healing process of the tubercular infection, and so require no special attention.

The tubercular process in the lung is particularly prone to mixed infection.

However, during the treatment of the tubercular condition, any of these pathogenic bacteria may get deeper lodgment and produce symptoms which will cause a drain upon the system. The progress against the tubercle bacillus will thus be interfered with unless treatment aiming to eradicate the mixed infection is instituted. Since the streptococcus is the most frequent offender in pulmonary mixed infec-

tions, a vaccine made of the streptococcus will often control all the annoying symptoms that may arise to interfere with the tuberculin treatment. Frequently, the catarrhal types of bacteria become just as annoying; thus the micrococcus catarrhalis, and the pneumococcus, and other bacteria occasionally demand our attention. In order not to deviate from the practical purpose of this book, I shall not go into detail here concerning the more infrequent infective organisms, especially as such bacteria are isolated and grown with difficulty. The streptococcus vaccine will cover so many cases of mixed infection that by means of this vaccine alone much can be done in the treatment of a mixed infection superimposed upon a purely tubercular process in the lung.

Primary mixed infections are most difficult to treat.

Mixed Infections Which Act as Fertilizer for the Tubercular Process. Primary mixed infections offer a more difficult task for the physician. Here we have a chronic respiratory infection as the primary pathological process—the process acting after the manner of trauma in bone and joint infection by establishing a localized loss of resistance, while the bacteria act as fertilizer for the growth of the tubercle bacillus when once the tubercle bacillus lodges in the respiratory tract.

A distinction must always be made between the symptoms produced by the tubercular process, and those produced by the mixed infection.

By careful differentiation between the various signs and symptoms, we can distinguish those symptoms which are caused by the mixed infection, from those due to the tubercular process. Unless this differentiation is made, the physical signs in these conditions which are usually spread over one or even over both lungs, will produce the impression of an extensive tubercular process, whereas in truth only a beginning tubercular infection exists. It therefore happens that during any treatment of the mixed infection which proves effective, the tubercle bacilli may disappear from the sputum, leading to the assumption that a cure of the tubercular process has been accomplished.

At this stage the patient is usually discharged from further observation, although it is well known how readily

a chronic respiratory infection will return. When the slightest recurrence of the chronic infection takes place the tubercular condition recurs because the hypersusceptibility still remains. In this class of cases we have the great army of sufferers who are not alarmed at their condition because of the long standing of their infection. They take their condition seriously only when tubercle bacilli are found in their sputum. A change of climate, and more favorable hygienic, dietetic treatment, quickly improve these patients. They then return to their regular habits and occupations, only soon to fall victims to a recurrence. The chronicity of the mixed infection thus goes hand in hand with the chronicity of the tubercular infection, the pendulum swinging back and forth between apparent cure and evident recurrence until they finally succumb to the slowly progressive tubercular infection, or to an acute exacerbation of the disease.

Treatment of the tubercular process is often relaxed on account of the misinterpretation of the disappearance of symptoms which were due to the mixed infections.

The tuberculin treatment of these patients we have already discussed in Chapter VI, Part II. If we add vaccine treatment for the mixed infection, we are able to raise the resistance of these patients to a degree that will permit a thorough eradication of the tubercular process. Since tuberculin also removes the hypersusceptibility, a recurrence is thus in a great measure prevented. Of course the ideal treatment is a combination of immunotherapy with climatic treatment, but when circumstances will allow only one of the two methods, immunotherapy must be chosen. The increasing of resistance through immunotherapy in spite of the patient's surroundings will produce permanent results, whereas a return to former conditions after an improvement gained through a change in climate will prove more rapidly detrimental than when those conditions contributed to the production of the original condition.

The chronic infections which prepare the soil for the advent of the tubercle bacillus may be any one of the chronic infections that exist in the respiratory tract, such as chronic bronchitis, bronchial asthma, unresolved pneumonia and all

catarrhal conditions that form pathological changes in any of the respiratory passages. The bacteria that are most at fault here are the streptococcus, micrococcus catarrhalis, the pneumococcus, m. paratetrogenus, Friedlander B., bacillus influenza, staphylococcus albus and aureus.

The medical treatment of respiratory mixed infections is important.

Treatment. The medical treatment and the hygienic dietetic treatment must be carefully carried out in chronic mixed infections, whether the mixed infection was the cause of the tubercular process, or came as a result of it. The indiscriminate use of drugs should be avoided especially in the case of narcotics or creosote. Creosote, when wrongly used, is capable of a great deal of harm, and yet, should not be dispensed with, for it is equally capable of a great deal of good when applied in the proper condition and in the proper dosage. We should familiarize ourselves with the physiological action and proper indications for the use of this drug before prescribing it.

The vaccine treatment of respiratory mixed infections.

The dosage of vaccines is the same in all chronic conditions. Fifty million of the streptococcus should be given as a beginning dose, increased by about twenty million for the following three or four doses and if there seems to be no beneficial effect—as would be noted by a decrease in amount, or a change in character of the sputum, or by an evident decrease of the streptococcus in the sputum—the last dose should be doubled and then continued at the same rate of increase as before.

The micrococcus catarrhalis and B. Friedlander best administered in doses of twenty-five million, increased by five or ten million for each of the subsequent four or five doses and if need be, the fourth or fifth dose can be doubled to get a more positive effect.

The beginning dose of the m. paratetrogenus should be fifty million, increased by from ten to twenty million at each subsequent dose.

The pneumococcus and b. influenza should be administered in the same dosage as the m. catarrhalis.

The staphylococcus albus and aureus should be administered in a dose of two hundred million in the beginning, with subsequent increases of twenty-five to fifty million, with the same doubling of the fourth or fifth dose if it should be necessary.

TABLE OF DOSAGE

	Beginning Dose	Increase
Streptococcus	50 million	20 million
M. Catarrhalis	25 million	5 to 10 million
B. Friedlander	25 million	5 to 10 million
M. Paratetrogenus	50 million	10 to 20 million
Pneumococcus	25 million	5 to 10 million
B. Influenza	25 million	5 to 10 million
Staphylococcus Albus / Aureus	200 million	25 to 50 million

Treatment of the mixed infection before tuberculin treatment.

Before tuberculin treatment is instituted it is advisable to treat the chronic infection with vaccines until it is under control. About three or four weeks of treatment will usually suffice to get the chronic infection under control, and then tuberculin treatment should be instituted. However, we must make certain that where vaccine treatment is instituted before the tuberculin treatment, the acute condition is not due to the tubercular infection. The tuberculin treatment should not be delayed in cases where the tubercular process has produced a great deal of wasting.

In case of a multiple mixed infection and if the patient is in fair physical condition, it is best to administer a separate vaccine of each organism on different days rather than to treat the patient with all of the vaccines at the same time. For the purpose of illustrating, let us assume that the streptococcus, the m. catarrhalis, and the pneumococcus are the principal offenders. The streptococcus vaccine can be administered on Monday, the catarrhalis vaccine on Wednesday, and the pneumococcus vaccine on Friday. A more clear cut immune response can thus be obtained, and

a more accurate observation can be made of the effect of each vaccine.

Treatment of the mixed infection during tuberculin treatment.

In chronic mixed infections which become implanted upon a tubercular area, vaccines need not be used until the tuberculin treatment has been administered for two or three months. The reason is the same as for the application of vaccines before tuberculin in primary mixed infections. The improvement of the primary condition through any agency will exert a beneficial effect on a secondary process. Through the treatment of the tubercular process which is here primary, the mixed infection process may be so favorably influenced that it may require no treatment. The local hyperemia produced by the tuberculin focal reaction is sufficient to overcome the mixed infection, especially as the chronicity of the process has robbed the causative bacteria of their virulence.

However, should the mixed infection persist in spite of improvement in the tubercular process, its treatment should be undertaken by the use of a vaccine against the most prominent organism found in the sputum. Later, a vaccine against each of the other organisms that persist in the sputum should be used, if no improvement has taken place from the previous vaccine. In the same manner several vaccines may be tried in turn until the mixed infection is no longer a factor in the production of symptoms. These vaccines should be administered once a week, and so timed that they do not interfere with the tuberculin reaction.

Acute Respiratory Mixed Infections

An acute mixed infection in a tubercular lung renders the prognosis grave.

Acute respiratory infection occurring in a patient with pulmonary tuberculosis forms a most serious condition of affairs, since an acute infection has the tendency to greatly lower the resistance of the patient to tuberculosis. When acute infection occurs in the same organ, it not only raises the hypersusceptibility to a marked degree, but also encourages a local extension of the tubercular process.

So it happens that a lesion erstwhile progressing favorably under tuberculin treatment may be suddenly invaded by an acute respiratory infection which lights up the tubercular process to such a degree that it passes beyond control. Fortunately, in prophylactic immunization we have a means by which the danger of an occurrence of acute infection can be greatly minimized. But when it does occur we must unite all the resources at our command to tide the patient over the acute attack. Since vaccine forms at least as important a measure as any other, it is the duty of every physician to utilize it under such urgent circumstances.

Acute mixed infections are of two varieties: 1. Acute exacerbations of a chronic infection; 2. Fresh acute or epidemic infections.

In dealing with acute pulmonary infections complicating tuberculosis, two distinct types should be recognized: the acute infections which are acute exacerbations of a chronic infection, and the fresh acute infections that are epidemic. Under the former, we are dealing mainly with pyogenic organisms producing such conditions as pulmonary abscess, empyema, and pneumonic processes. Under the second class, we deal mainly with catarrhal bacteria producing acute "colds," influenza, and so on.

Treatment of acute mixed infection in respiratory tuberculosis.

Treatment. Aside from immunotherapy for acute conditions in pulmonary tuberculosis, we can add but little to the present day accepted methods of treatment. However mild the acute infection may be, rest in bed is absolutely imperative. Appropriate drugs, proper food and proper elimination are equally important. However, a wider experience with immunotherapy will not only demonstrate its value as an additional aid in the treatment of acute respiratory infections, but the reduction in the frequency of the occurrence of acute infection through prophylactic immunization will become apparent.

Interrupt tuberculin treatment during the treatment of acute infection.

During the vaccine treatment of acute conditions it is best to interrupt the tuberculin administration while the process is still acute. The increased hypersusceptibility that occurs as a result of the acute infection may bring about a constitutional reaction which, being masked by the symp-

toms of the acute mixed infection, would lead to a further increase in the dose of tuberculin, and bring about a disastrous result. After such an interruption, the tuberculin treatment should be resumed with a dose considerably smaller than the last dose previous to the acute infection.

The bacteria most concerned in acute infections are: the pneumococcus, M. catarrhalis, M. tetrogenus, B. septus, B. influenza, the staphylococcus, and the streptococcus.

TABLE OF DOSAGE

	Beginning Dose	Increase
Pneumococcus, M. Catarrhalis, M. Tetrogenus, B. Septus, B. Influenza	25 million	5 to 10 million
Streptococcus	20 to 40 million	10 million
Staphylococcus Aureus	100 to 150 million	
Staphylococcus Albus	25 to 50 million	

The temperature curve is the best guide to dosage and intervals of vaccine treatment.

In the treatment of acute infections with vaccines we have the temperature curve as the best guide to dosage and intervals. A careful temperature record will show at the end of twenty-four hours whether the dose was insufficient, or whether an overdose was used and a negative phase produced. The vaccines of all the offending organisms should be administered in each inoculation, unless the infection definitely points to one or more of the bacteria as being the sole cause, in which case these alone should be used and the rest ignored.

One example is the pneumococcus: If the sputum shows an abundance of the pneumococcus, a vaccine of the pneumococcus will be sufficient even though other bacteria may appear in the smear; the same holds true of the influenza bacillus. However, if the streptococcus or the M. catarrhalis appear with the two mention eria, it can

do no harm, nor can it jeopardize the beneficial effects derived from the use of the influenza or pneumococcus vaccine if we add the minimum doses of streptococcus or M. catarrhalis vaccines. After the acute symptoms are passed, it is advisable to continue the use of the vaccines for several months at weekly or two-weekly intervals.

Prophylactic Immunization Against Mixed Infections

Prophylactic immunization against mixed infections plays an important part in the treatment of pulmonary tuberculosis.

Vaccines have no better field than in prophylactic immunization against mixed infections in pulmonary tuberculosis. We all know the importance of protecting these sufferers against weather changes and against exposure to rain and dampness. We also realize that the object in carrying out these measures of protection is to prevent a temporary lowered resistance, which would render the individual subject to a new bacterial invasion, or to an acute exacerbation of chronic infection.

But what is the success of these measures? In spite of all that is done, there are so many chances for the patient to be caught off guard, that only few escape an infection in the respiratory tract during the treatment of the tubercular condition. Prophylactic immunization greatly reduces the dangers of infection by raising the resistance to the bacteria to such a degree that even if it is not sufficient to prevent infections altogether, it certainly will prove effective in combination with the usual measures of prevention.

The importance of prophylactic immunization against mixed infection cannot be sufficiently emphasized. Among the greatest achievements in medicine, that brought about by prophylactic immunization stands preëminent—I need but mention the prevention of typhoid fever alone, to call forth a realization of the possibilities of prophylactic immunization. The written medical annals of the present great war will contain no less a staggering array of superwonders brought about by medical and surgical skill, than those

accomplished by the engineer or general. And prophylactic immunization against all forms of infection will be found to have played a startling part in the formation of these annals. I say *startling,* because the greater part of the medical profession that still scoff at vaccine therapy in general, will suddenly wake up to the fact that they have been hopelessly left behind.

The following two forms of prophylactic immunization should be considered:

Prophylactic immunization consists of two distinct forms: that which aims to prevent epidemic infections, and that which aims to prevent acute exacerbations of infections the bacteria of which are present in the sputum.

1. Prophylactic immunization against epidemic infection.

Prophylactic Immunization Against Epidemic Infections. Prophylactic immunization against epidemic infections is as simple as prophylactic immunization against typhoid, except that we have more than one bacteria to deal with. As in typhoid, three inoculations with a stock vaccine are administered a week apart, and in the following doses:

	First dose	Second dose	Third dose
Pneumococcus B. Influenza M. Catarrhalis B. Friedlander Streptococcus (Salivarius)	100 million	200 million	300 million

A bottle of stock vaccine (holding from five to twenty cubic centimeters) should be obtained of each bacteria. A concentration of at least 1,000 million bacteria per cubic centimeter should be insisted upon, thus avoiding too bulky an inoculation for the third dose.

The five bacteria need not be combined into one vaccine and administered at one time. If it is found expedient, we may divide them into two groups and administer one group on one day, and the other group on another day, keeping a record of the administration of each so that the reinoculations may be continued at weekly intervals.

Prophylactic Immunization Against Acute Exacerbations. Prophylactic immunization aimed to prevent acute exacerbations of infections, the bacteria of which are present in the sputum, is not quite as simple as the prophylactic immunization against epidemic infections, as it requires a microscopic study of the sputum in order to determine the bacteria against which immunization is necessary. However, the amount of knowledge that is required for practical purposes can be acquired without much difficulty. The organisms that need be considered in this connection can easily be distinguished after a short reference to any book on bacteriology, especially Allen on "Bacterial Diseases of Respiration." The organisms consist of one or more of the following bacteria, and should be administered according to the accompanying dosage:

2. Prophylactic immunization against acute exacerbations of existing chronic infections.

	First dose
Pneumococcus M. Paratetrogenus M. Cattarrhalis Streptococcus (Salivarius) B. Friedlander	50 million, increased weekly by 25 million

One inoculation a week is sufficient, but inoculations should be continued for a longer period than in the case of prophylactic immunization where the bacteria are not present in the sputum.

In the estimation of the value of prophylactic immunization we must consider the length of the period of immunity that is conferred by the various infectious organisms. It is well known that these periods differ greatly with the different infections. For instance, the bacteria producing measles confers a life immunity; in the case of typhoid, the period seems to be about seven years; in the case of diphtheria, the use of prophylactic antitoxins seems to protect for about six weeks only, and so on through the various infections. Un-

The length of time the bacteria are capable of conferring an immunity should serve as a guide for re-immunization.

fortunately the length of immunization acquired as a result of respiratory infections seems to last no longer than two or three months. Therefore, it is necessary to repeat the prophylactic immunization once or twice during the period between September and May. For example, if a prophylactic immunization is administered in September, it is advisable to repeat the inoculations in December and again at the end of February.

General Prophylaxis

The disregard of important prophylactic measures is particularly noticeable in the treatment of pulmonary tuberculosis. This is true not only in ambulatory cases, but in cases treated in many public institutions.

The consideration of prophylactic measures apart from vaccines does not come under the province of this work, but I find that the neglect of prophylactic measures is so frequently a source of failure in immunotherapy that I cannot dismiss the subject without calling attention to its importance. The more recent adoption of prophylaxis of the mouth and teeth and nasopharynx into general prophylaxis also deserves more attention than it receives at the hands of the general practitioner; especially when its main object is to remove common sources of reinfection. Here also we shall take into consideration the elimination of pathological processes which so frequently occur in obscure recesses and occupy such small areas that they escape the notice of the patient as well as of the physician. The consideration of dietetic measures, not only from the standpoint of nutrition, but what is more important, from the standpoint of assimilation, must be here included as well as the important elements of rest and exercise.

Attention to the nose, throat, and periodic dental examinations will remove conditions which are most frequently the source of mixed infection.

Elimination of Sources of Infection. One of the principal contributions to the knowledge of medicine in the last decade has been the discovery that pathological dental processes, pathological changes in the tonsils and in the nasal pharynx form important factors in the production of chronic disease, and that the elimination of these factors is essential to the total eradication of chronic infections. Since tuberculosis is the most universal of the chronic infections,

these pathological processes demand as much attention when they ocur in a case of pulmonary tuberculosis as in any other chronic infection. A thorough examination of the teeth and gums by a competent dentist, including X-ray examinations of the dental processes and of the roots, is a necessary adjunct to the successful treatment of tuberculosis.

The bacteriological study of tonsils removed from otherwise healthy children has sufficiently demonstrated the fact that the tonsils are not only very often the source of mixed infections, but the source of the tubercular process as well.

The nasopharynx, including the sinuses and antrums, is a frequent source of mixed infections. We may not, however, institute indicated surgical measures such as the removal of adenoids, the removal of tonsils, the removal of hypertrophied turbinates, etc., until the tubercular infection has been checked. But during the treatment of the tubercular process we must institute such measures as will eliminate their negative influence on the favorable progress of the disease.

We often cannot dispense with the dentist in spite of the poor circumstances of the patient, but we are able to administer such medical treatment for the various conditions in the nasopharynx, etc., that in these conditions we can for the time being, at least, dispense with the help of a specialist. Of course it would be ideal to have a specialist co-operate with us in the treatment of these conditions, but the majority of us deal with a class of patients that cannot afford any extra expense, and a large number of general practitioners who practice in the rural districts are beyond the reach of the specialist.

A nasal spray composed of twenty grains of menthol, twenty grains of camphor, a few drops of oil of cinnamon in an ounce of liquid vaseline will do a great deal to improve the breathing and is as good a mucous membrane antiseptic as we have. Add to this a five to twenty per cent. argyrol, and our armamentarium is complete for the control

of most of the conditions that may exist in the upper air passages. Other medicaments for local application or for internal use may be found of value for special conditions. For further detail the reader is referred to the proper authorities on the subject.

Personal hygiene must be insisted upon.

Personal Hygiene. Personal hygiene of the patient embraces daily care of the mouth and teeth and frequent bathing to enlist the proper function of the skin. Let me mention here that the matter of encouraging bathing is of great importance, as the fallacy exists among the laity that the bath is detrimental to the sufferer from phthisis by exposing him to colds. He should be encouraged to live under proper conditions, a clean room, proper ventilation and many other fine details that are not only beneficial from the hygienic standpoint, but help to divert the patient's mind to details not altogether bearing directly on his disease. These diversions are very helpful. I mention these very familiar points in the hygiene of the patient, not because I need to call attention to them,—that is hardly necessary in view of the fact that the importance of hygiene in tuberculosis was recognized generations ago and constitutes practically the major part of the usual treatment of tuberculosis—but in order to call attention to the absolute necessity on the part of the physician to insist upon their being carried out. Frequently these directions for hygiene are given to the patient at the same consultation when his diagnosis is made and when the patient's mind is far from realizing their importance. Again, the patient reads and hears so much about hygiene that his very familiarity with the subject causes him to neglect it. The physician must repeat his directions and insist on absolute compliance with them, and refuse the treatment of any patient who persists in neglecting them.

Dietetics. Dietetics in tubercular individuals has been a topic of controversy for many years. The varied opinions of different workers in tuberculosis have extended from rest

in bed and fluid diet to the extreme of forced feeding. I believe we have at last arrived at the best possible method of feeding tubercular patients. Tuberculosis is a disease of long standing and slow wasting. It should be our object to push the nourishment to the maximum point of tolerance; but absolutely limited by the amount of assimilative powers of the individual. As soon as we exceed the power of assimilation by any quantity of food, we throw an added burden upon the already over-taxed system by forcing it to dispose of the surplus. And since the circulation must be drawn upon in order to dispose of any surplus food, the circulation is diverted in an undue degree to the gastro-intestinal canal, and an anemia is created at the point of infection. Improper feeding will thus interfere, or wholly prevent one of the main assets in the conquest of disease—hyperemia.

Dietetics must be regulated according to the assimilative powers of the individual.

It is not difficult to estimate a patient's assimilative powers. Symptoms like distress in the stomach, fullness, sleepiness and dullness in the head after meals, languidness, all point to over-feeding. The rapid accumulation of fat should not be looked upon without apprehension. Such a gain in weight does not indicate a gain in strength and resistance. On the contrary, a rapid accumulation of fat such as is indicated by a rapid gaining of weight without an increase of strength, points to a process of surplus food disposal which some patients acquire as a protection against stagnation, but which requires an unusual drain on the circulatory mechanism. Hence a circulatory insufficiency at the infected area is followed by the retrogression that is so often noticed in such patients under the least adverse circumstances. Nourishing food and well masticated, in quantities easily assimilated, and proper bowel action, are the essentials of proper dietetics for the tuberculous individual.

The following three radiographs of pulmonary conditions will be found interesting in connection with diseases of mixed infections. They represent three distinct types of tubercular pulmonary disease modified by mixed infection.

The first, Fig. 46, represents a mild tubercular condition lasting over a period of two years with very little pulmonary destruction. A hemorrhage was the first sign of the disease followed by a persistent but mild cough. Bacilli did not appear in the sputum So few were the physical signs in the lungs that my diagnosis of pulmonary tuberculosis made at the time of the hemorrhage was severely criticized and denied by five physicians under whose treatment the patient came during the two years. At the beginning of the third year, the cough began to increase and became productive for the first time. The amount of expectoration steadily increased in quantity and became more and more purulent in consistency. Abundant tubercle bacilli were now demonstrated in the sputum, a circumstance which brought the patient back under my care. The physical signs were those that point to the condition as shown in the X-ray photograph, Fig. 46. Although both apices were the seats of considerable cavities, the rest of the lungs is clear. The mild apical lesion became the seat of mixed infection with the formation of a true abscess in each upper lobe, causing rapid disintegration of the tubercular tissue and remaining the seat of a constant purulent production. Without mixed infection treatment, tuberculin, while it may prevent the spread of the disease beyond this localized area, cannot stop the pus formation in the cavities, nor distressing symptoms which it produces.

The second, Fig. 47, represents a more widely distributed tubercular process. The tubercular infection began after a grippe infection; the cough, which was mild, persisted for a year and a half with but slight expectoration. The patient, however, lost rapidly in weight and in strength, night sweats were persistent —in short, he presented a typical picture of pulmonary tuberculosis of the slowly progressing type. Towards the end of the second year of his illness an attack of grippe brought about alarming symptoms including a severe hemorrhage, and the patient was removed to a high altitude where after three months of treatment and rest in bed, the

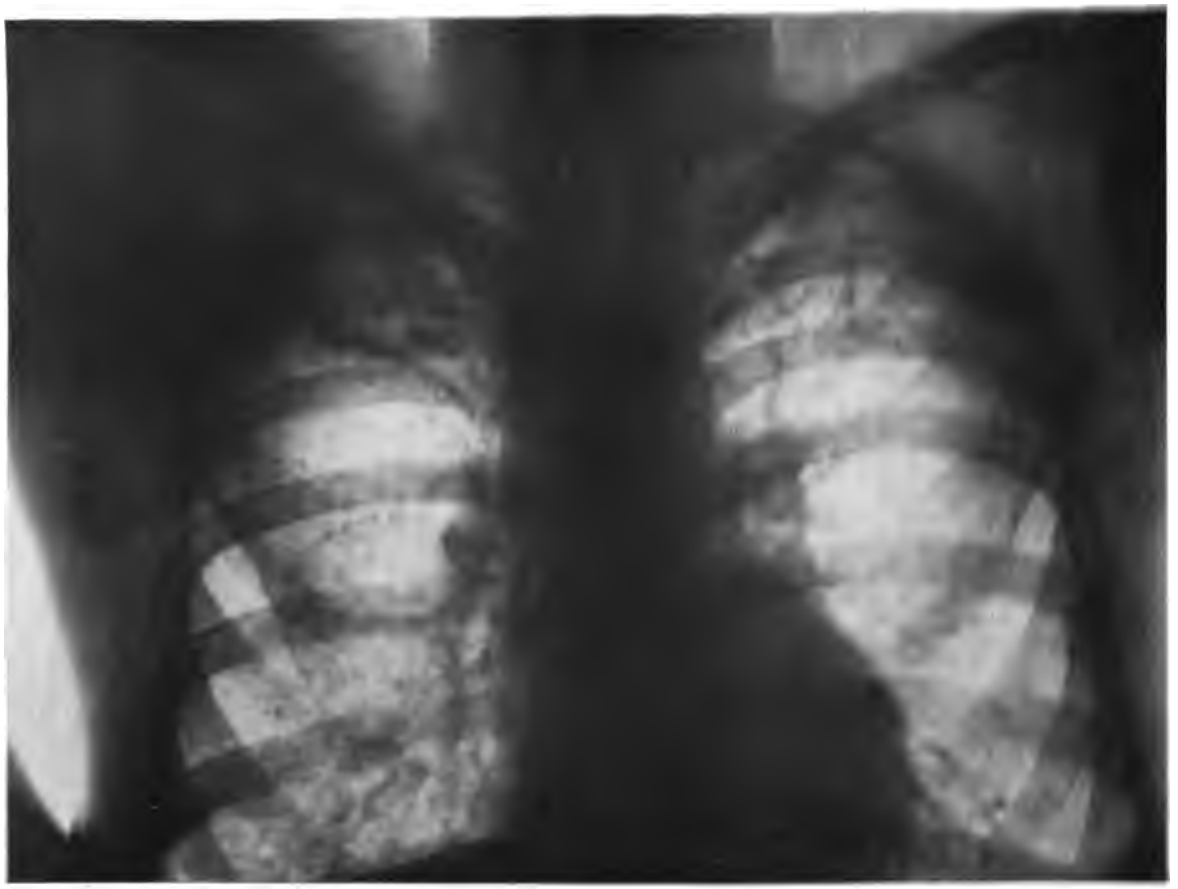


Fig. 46—X-ray of Chest—Circumscribed Mixed Infection

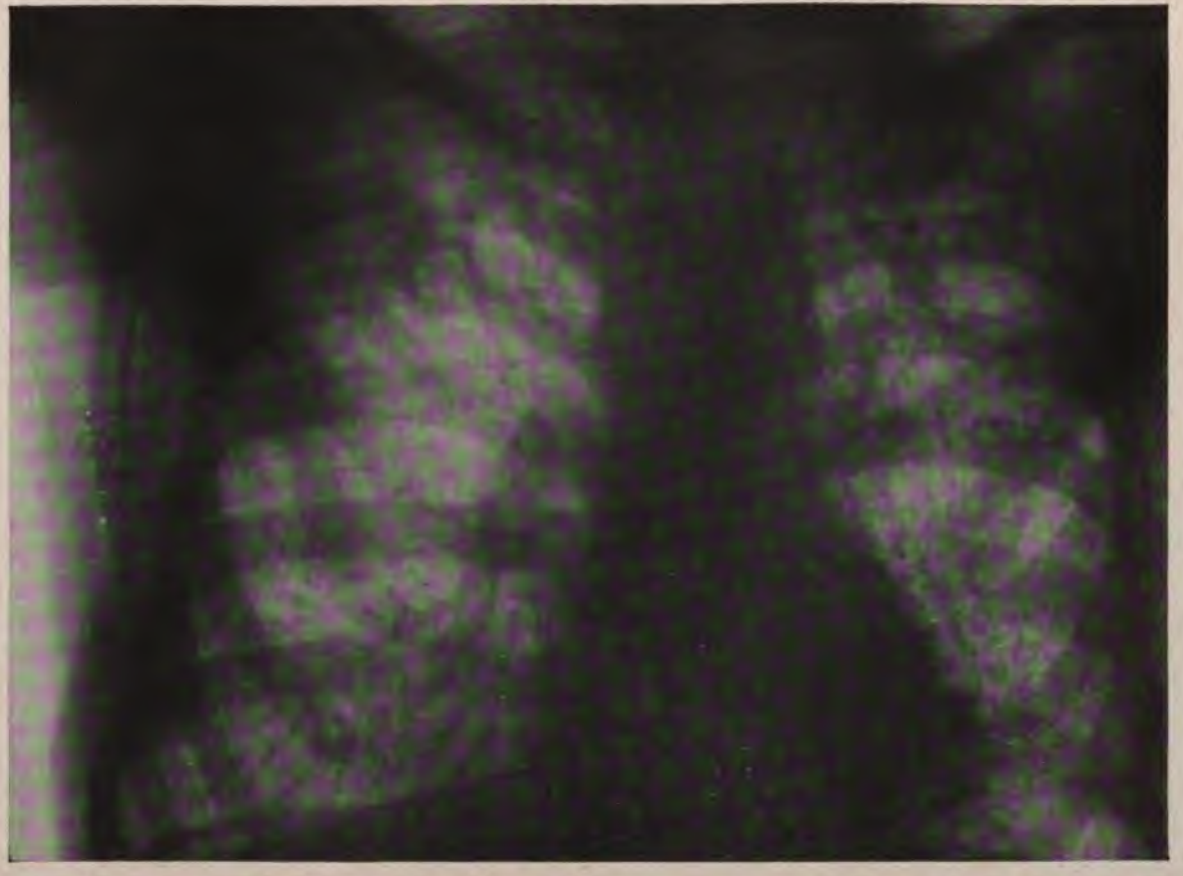


FIG. 47.—X-ray of Chest—Slowly Progressive Tubercular Lesions, the Mixed Infection Preventing Complete Healing.

acute symptoms subsided, but the amount of cough and expectoration increased to such an extent that it interfered with the patient's sleep, and frequently brought on attacks of vomiting. The patient was then sent to Denver, Colorado, where he gained in weight and improved in every way except in the amount of cough and expectoration. He returned and applied for tuberculin treatment at the New York Polyclinic Hospital.

As will be seen in the radiograph, the left lung is the seat of a cavity in the upper lobe near the apex, and although there are small foci of healed tuberculosis throughout, the lung is the seat of compensatory emphysema. The fact that there is a contracting cicatricial form of healing in the left lung with compensatory emphysema in the right, is sufficient evidence that the patient possesses a fair amount of recuperative power. But the mixed infection interferes to the greatest extent with the complete arrest of the process. Under mixed infection treatment and tuberculin administrations, the patient has improved far more rapidly than under special climate and sanitarium treatment. After the first month of immunotherapy the patient returned to work and has never lost a day for the last three and a half years.

The third, Fig. 48, illustrates a case of a tubercular infection following upon a fertilized field prepared by a ten-year-old chronic bronchial infection. The amount of hypersusceptibility was never high so that the tubercular process was never acute. The following is a copy of the X-ray report made when the patient first applied for immunotherapy in December, 1915.

> Radiographic examination of your patient, X, shows a marked degree of involvement of practically all of both fields. There are large cavities in the left upper lobe. All the costal cartilages are markedly calcified, and there is little evidence of calcific deposit in the pulmonary fields.
>
> Doctor Y.

A year later the following radiographic report was made of his condition, which is an interpretation of the third radiograph here illustrated (taken in November, 1916).

Radiographic examination of your patient, X, shows a marked degree of clouding and infiltration of both pulmonary fields. The upper third of the left pulmonary field is consolidated. There are bands of adhesions and a portion of a cavity wall in the middle of the left pulmonary field. The right pulmonary field shows a moderate degree of compensatory emphysema. The cardiac shadow is drawn to the left.

Doctor Y.

In 1913, the patient had a very serious hemorrhage followed by a long confinement in bed. In 1915, or just prior to the beginning of tuberculin and vaccine treatment, the patient suffered an acute exacerbation of the mixed infection with high temperatures, causing extreme emaciation and confinement to bed for two months. It was at the earnest solicitation of the patient's family that I undertook his treatment. They wanted him to have every comfort and hope for the last months of his life—the patient being fully aware of the hopelessness of his condition. His history, together with an examination of his sputum, revealed to me the fact that a mixed infection was responsible for the most distressing symptoms—cough which was racking and constant especially at night, and expectoration which was purulent and very profuse. The patient ran an afternoon temperature of 100.5 to 101.5.

Improvement commenced after two months of treatment with tuberculin and vaccine. After six months of treatment, the tubercle bacilla disappeared from the sputum. The cough became less severe during the day and disappeared entirely during the night. Fig. 48 is a radiograph of the patient's chest at the conclusion of treatment. The patient is greatly improved and at this writing (six months later) is still maintaining his improvement.

A comparison between the two reports shows a definite structural improvement as well as a symptomatic improvement. I did not publish both radiographs because I did not intend to show structural changes at this point, I merely publish the last radiograph in order to show that even in such an apparently hopeless condition, the combined vaccine and tuberculin therapy can do much to improve a patient.

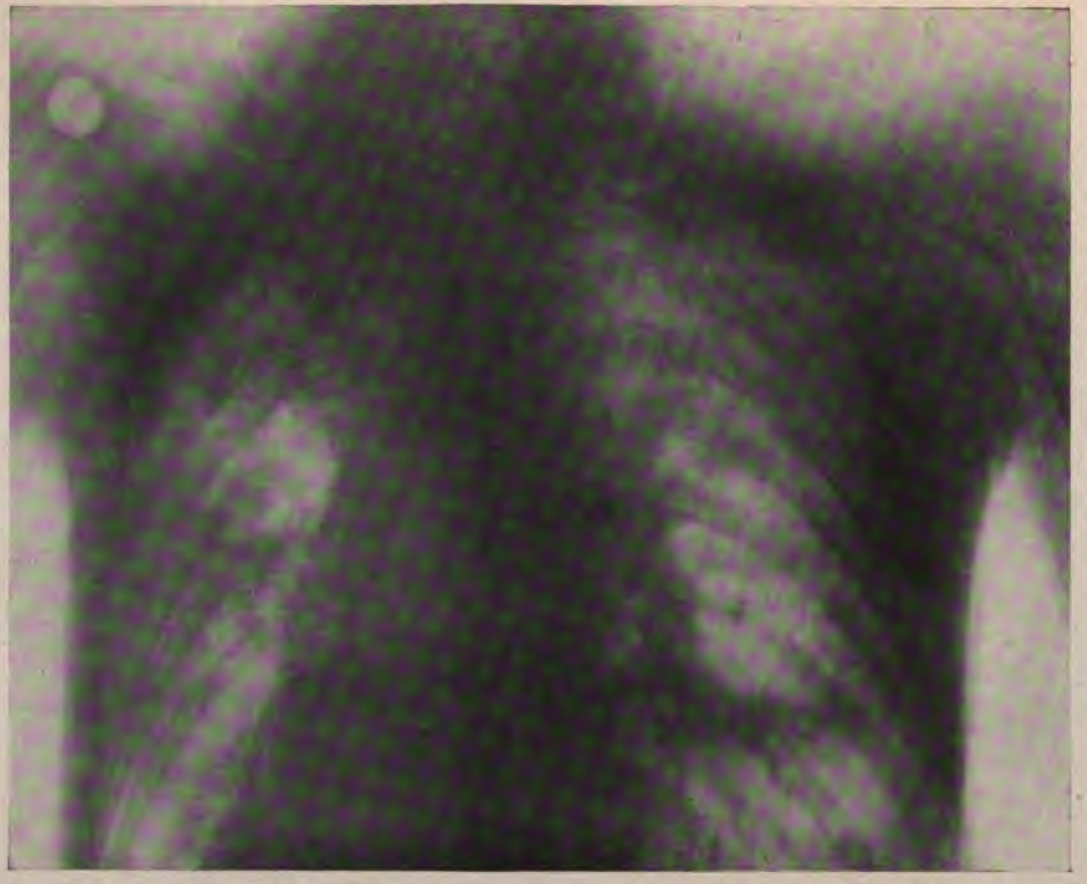


FIG. 48—X-ray of Chest—Tubercular Process Superimposed upon a Chronic Mixed Infection.

Chapter VI

SURGICAL MEASURES

To be absolutely correct, this topic should be headed "Tubercular Surgery," for experience has revealed the fact that surgical principles as applied in general surgery do not apply in like manner in tubercular surgical conditions. Hardly a day passes without bringing further evidence that general surgery when applied in tubercular conditions does more harm than good and sometimes irretrievably injures the patient. One main reason for the unique situation that tubercular processes offer, from the surgical point of view, is the fact that the tubercle bacillus is not a pyogenic organism, and that its infective process is in the main extremely localized. The action of the tubercle bacillus is entirely local, its spread means an involvement of a larger area but still localized. It produces no effect in the blood circulation; and when the tubercle bacillus does get into the circulation it may lodge in glandular structure distant from the point of infection and become localized there.

Surgical principles must be greatly modified in their application in tubercular conditions.

All this occurs very slowly. So slowly, in fact, that the natural resistance of the body against the tubercle bacillus is able to localize or limit the infection. And it is only after a long standing immune response bringing about a high grade of hypersusceptibility that we may get a general, disseminated tuberculosis. That is extremely rare; and when it does occur, we know that it comes more frequently after radical surgery than when surgery, however necessary and conservative, has been altogether withheld. In fact, in tuberculosis, from the standpoint of surgery, conditions hold true directly opposite to those that apply in other infections. For instance, in other infections surgery will prevent a general septicemia, and will prove effective in proportion to the promptness of its application. In tubercular infections, on the contrary, general infection occurs in direct proportion

to the amount of surgery applied. Hence, the entire neglect of surgery has rarely produced a general dissemination of the infection.

The principal reasons for surgical interference are:
1. The prevention of undue destruction.
2. The modification of symptoms.

The whole subject of surgery in tuberculosis can therefore be limited to its application as a means to reduce symptoms and prevent extensive localized destruction. In fact, the most important reason for its application is for cosmetic effects.

Most of the infected areas will finally break down and drain by means of fistulas. However, there is a great deal of pain until that occurs, hence, the application of surgery for the purpose of forestalling extensive destruction and for the amelioration of pain.

On the other hand, we must not overlook the importance of proper surgery in tubercular conditions for cosmetic effects. Breaking down of tubercular processes produces ugly scars, and by getting ahead of such breaking down with the proper surgical interference, we may prevent the formation of scars, or we may at least reduce them to a minimum.

Nature's effort to localize all tubercular infections must not be interfered with by surgery.

The extensive operations that have been recently devised for restoration of function, for the limitation of progressive deformities, or for the removal of parts where the destruction has gone beyond the possibility of restoration of function, should be applied only after the hypersusceptibility of the individual has been removed by a course of tuberculin. In this way, we remove all possibility of the extension of the process beyond the radius of the surgical interference. In other words, with tuberculin we remove the constitutional element of the disease, and by limiting the process to a local condition we endow the necessary surgical measures with the highest degree of safety.

In order to successfully apply surgery in a tubercular individual, we must always bear in mind that it is the hypersusceptibility and not the tubercle bacillus that is the cause of any extension of the process; and that in applying surgery to abscesses, fistulas, tubercular glands, etc., we are doing so merely to produce a better result than would occur

by natural processes alone. To sum up, if we wait with the major surgery until we have eliminated the hypersusceptibility with tuberculin, and limit the surgical measures to the treatment of the resultant local tissue changes, we will be rewarded with a commensurate degree of success.

Before entering upon the chapters dealing with the surgical treatment of tubercular infections of glands, bone, etc., the nature of the various processes involved in tubercular areas must be clearly understood. These consist of the following four distinct forms:

The following four local tubercular manifestations must be borne in mind in relation to surgical measures. 1. Pure tubercular infiltration, leaving no gross alteration on healing; 2. Fibrosis, which leaves behind a mass the size of which is in proportion to the extent of the original process; 3. Tubercular inflammation altered by mixed infection; 4. Encapsulation plus liquefaction, or cold abscess

The first is the pure tubercular process which in healing becomes absorbed, disappearing entirely for the most part.

The second is the process of cicatrization. A tubercular area may be filled in with connective tissue forming a hard cicatrix. This may or may not become impregnated with calcium salts. Depending upon the extent of the original process, it may on healing, leave behind an area of altered structure which if near the surface, forms a palpable mass.

The third is a tubercular process modified by mixed infection, which brings about a slow suppuration with pus formation.

The fourth is a process of liquefaction within a protective capsule surrounding the original tubercular area. This liquefaction might remain unchanged for a long period. It is known as "cold abscess." However, the cold abscess may become infected and change to the suppurating variety by breaking through to the surface. Again, it may terminate by the secretion from the cells lining the wall of a tryptic ferment, which, acting as a digestant upon the capsule walls and finally on the tissues beyond, breaks upon the surface and expels its contents.

This process of "pointing" of a cold abscess through the digestion of tissue must be distinguished from the "pointing" of inflammatory abscesses through suppuration. The former process is sterile, therefore much slower; and when the surface is approached, there is a direct sloughing of tissue instead of mere breaking open as in the case of ordinary abscesses.

Chapter VII

THE SURGICAL TREATMENT OF TUBERCULAR GLANDS

Classification: 1. Soft glands. 2. Suppurating glands. 3. Cicatrized glands.

The classification of glands with relation to their surgical treatment differs from the classification with regard to the tuberculin treatment. Whereas the one classification bears upon the relation of glands to the constitutional manifestation of the disease, in the present classification we must consider the nature of the local process in relation to local treatment. Thus we distinguish three varieties: the soft glands, the suppurating, and the cicatrized.

Soft Glands

Soft glands are the same in structure as cold abscesses.

Soft glands are cold abscesses. The gland capsule remains intact while the parenchyma becomes liquefied during the tubercular process. This liquid is mucoid in character and is interspersed with particles of caseous material. The older this cold abscess, the less of this caseous material floats in the fluid, for the caseous material precipitates towards the wall of the abscess and organizes into a false membrane of varying thickness depending upon the amount of the caseous material originally present. This liquid is free from mixed infection and rarely contains the tubercle bacillus. It practically forms a healed tubercular area, although the individual may not be free from tuberculosis. Any active tubercular process in the same individual will appear in neighboring glands or elsewhere, but the cold abscess represents a healed process.

Treatment consists of puncture or aspiration.

The only treatment necessary for this form of glands is puncture or aspiration.

With a drop or two of one-fourth of one per cent. of cocaine, or one-half of one per cent. of novocaine, injected with a fine hypodermic needle intracutaneously over the part

of the gland nearest the surface, the incision may be rendered painless. The incision consists of nothing more than a puncture by means of a sharp pointed scalpel, the blade being no more than an eighth of an inch wide. If the liquid does not escape through this incision, a circumstance extremely rare, the incision may be widened, or a little sterile normal saline solution injected by means of a sterile dropper will render the contents of the gland sufficiently fluid to escape. A little sterile olive oil should then be injected to prevent contact between the opposite walls of the capsule and a small cotton collodium dressing applied.

FIG. 49

If aspiration is resorted to, a fairly large-sized needle should be used, the contents aspirated, and before withdrawing the needle, a few drops of sterile olive oil should be injected into the sack.

Frequently the needle tract will remain open, causing a narrow fistula, and creating the same condition as produced by puncture. This should not be considered detrimental. On the contrary, the sack may be re-emptied of any re-accumulation, by the use of the eye-end of a needle or even with a toothpick dipped in iodine, pushed into this fistulous tract. With an ordinary eye dropper a few drops of sterile olive oil should be injected after each time the sack is emptied, in order to prevent the rubbing of the surface of the sack,—thus preventing re-accumulation of secretions.

Strict asepsis is necessary.

Every step of this treatment must be carried out under strict asepsis. By the use of iodine on the skin, the aspirating needle will carry no infection within; and by the use of a little collodium dressing or alcohol compress over the

puncture, subsequent infection of the cold abscess will be avoided.

Both puncture and aspiration are carried out mainly to get ahead of the process of tryptic digestion which is bound to set in when a cold abscess existed for any length of time. Ugly scarring has resulted from the sloughing of the skin over cold abscesses through the process of tryptic digestion.

Aspiration may be repeated until no reaccumulation takes place.

If we succeed in getting ahead of the tryptic ferment formation, the re-accumulation of secretions will become less and less, until the sack becomes contracted upon its more solid contents, that is, the caseous false membrane, which now forms the only contents of the contracted capsule. The contents may be slowly forced out by the further contraction of the capsule and complete healing take place; or it may form a nodule forced out upon the surface of the skin which heals beneath. The nodule dries and eventually falls off just as a scab does, leaving a whitish scar beneath.

Suppurating Glands

Suppurating glands are local pyogenic abscesses prolonged by the tubercular process.

Suppurating glands are tubercular glands which have become infected with a pyogenic organism, usually the staphylococcus. Here we have a tubercular process rendered active by mixed infection, and an ordinary abscess formation continued by the tubercular process.

Occasionally the removal of the mixed infection will be sufficient to cause the healing of the tubercular process without any other treatment. However, in most cases a course of tuberculin will do away with the tubercular process and will suffice to bring about a healing by removing the very element that prevents the natural termination of a staphylococcus abscess. It is advisable to resort to the latter means of treatment first as the former does not do away with the tubercular hypersusceptibility, and a local recurrence or a new tubercular infection elsewhere may take place.

In the treatment of suppurating tubercular glands, the

tuberculin inoculation may suffice. We need not bother about a vaccine for the mixed infection until it becomes evident that the mixed infection is deep-seated and requires special treatment for its elimination.

Special treatment is not often necessary.

If during the treatment with tuberculin the first dilution has been reached without having produced any effect upon the local process, a vaccine treatment for the mixed infection should be undertaken.

Cicatrized Glands

Cicatrized glands are glands enlarged by the tubercular process and healed by the formation of scar tissue. In other words, healing has taken place by fibrous tissue degeneration.

Cicatrized glands are glands that heal by fibrosis.

This process of healing of tubercular glands unnecessarily forms a discouraging feature in tuberculin treatment. To the patient the palpable gland means the persistence of the disease and occasionally even the physician may not realize that fibrous healing may take place in glandular tuberculosis as in lung tuberculosis, and that fibrous healing in glands may leave them palpable or even as large as they were during the height of the infection.

I therefore call particular attention to this form of healing of the tubercular process; so that we may not underrate the tuberculin treatment when this form of healing occurs in a case of tubercular glands. For here, just as in bone and joint tuberculosis, we cannot expect tuberculin to eliminate the results of the tubercular infection while it eradicates the infection itself.

Special treatment is almost always necessary.

After the disease has been converted into a purely local process by means of immunotherapy, the following methods of treating the local condition may be resorted to:

First, we may inject substances within the glandular stroma in order to soften the fibrous tissue, by producing a destructive or cauterizing process.

Second, we may remove what remains of the glands through surgical interference.

Softening of the fibrous mass by means of chemicals.

Softening of the hard cicatrized glands may be brought about by the injecting of iodine or synthetic guaiacol into the center of the gland; or even a drop or two of carbolic may be injected through a hypodermic needle, using alcohol on the surface of the skin to prevent burning. After two or three injections, about a week or two apart, the gland will begin to soften and may be treated as a soft gland. The following formula will be found useful for this purpose:

℞	Synthetic guaiacol Merck,	gm.	6
	Metallic iodin,	"	3
	Sodium iodid,	"	6
	Glycerin,	"	30
	Saccharin,	"	0.50
	Distilled water,	"	10
	Misce et solve.		

Conservative removal.

When resorting to surgical measures in the treatment of cicatrized glands, radicalism is unnecessary. Tuberculin has eliminated radical surgery in tubercular processes, particularly in tubercular glands; and once hypersusceptibility has been removed, new tubercular processes need not be feared. Under local anesthesia and through the smallest possible incision, the gland can be easily separated from its surrounding tissue by blunt dissection or scissors. The incision may be closed by subcuticular suture.

Where there are several enlarged glands, it is best to make a separate incision for each, instead of using one large incision for the removal of all the glands. A large gland may be removed by morselation through a small incision.

Chapter VIII

BONE CAVITIES, SINUSES AND FISTULAS

Bone infection is synonymous with chronicity.

Infection of bone is synonymous with chronicity. The nature of bone tissue precludes hyperemia from the point of infection; hence, the insufficient immune response during the infection, and the retarding of anabolism through insufficient blood supply during healing. Again, while in the case of soft tissue the destroyed tissues escape in the form of pus, in the case of bone, the products of infection remain solid, forming sequestra which make the escape of destroyed tissue difficult or impossible. We are here dealing with a foreign body, which in addition to the infection contributes materially to the chronicity of the process.

The formation of fistulas and sinuses.

Even without the formation of sequestra, the healing of bone tissue and the formation of new bone is so slow that wound discharge takes place for a considerably longer time than in soft tissue. The route through which these products of infection are discharged must remain open for long periods of time. Assuming a similar function to that which natural canals possess for the discharge of excretion, these passages become lined with a granulation tissue layer, which is protective by preventing the closure of these channels. The result is the formation of fistulas and sinuses.

A combined treatment is essential.

The treatment of tubercular bone and joint disease must embrace besides the eradication of the tubercular infection, which was discussed in Part II, the elimination of mixed infection and the restoration to as nearly normal a condition as possible the structural changes that have taken place as a result of the tubercular infection.

Mixed Infection

Mixed infection in cases of tubercular bone disease differs in but few respects from mixed infection in other tuber-

The utilization of the immune response is hampered by a lack of hyperemia.

cular infections. The difference can best be understood if we bear in mind that we have to deal with an inferior blood supply when the immune response is utilized in treatment of bone infections. Once we have this fact established, we are ready to employ infinite patience in the treatment of bone disease.

What is more, there is nothing to impede our progress once we start, for this class of patients will permit all the time and experimentation that a course of treatment requires. All they wish in return is a reasonable hope for an eventual cure. For of all tubercular cases these are the most pitiable. Although their lives are not threatened, and although in most other respects they are physically well, still their condition stands between them and self-support,—often between them and self-respect. For the tender care and sympathy extended to the sick spends itself in time, leaving these patients to the monotonous routine of daily dressing their wounds and obtaining their livelihood as best they can. In any case they are a burden to their families, and often to the community. This is the hopeless condition in which these sufferers approach us. So that it is no wonder that any hope of cure will be welcomed, no matter how much time or experimentation it involves. That is why the element of time does not have to be seriously considered in a course of treatment such as bone tuberculosis requires.

Treatment. After the tuberculin treatment has been applied for a week or two, it is advisable to begin the treatment for the mixed infection, proceeding as follows: A smear of the pus is made, and stained with methylene blue for the diagnosis of the organism causing the mixed infection. If no bacteria are found, a further test as to the sterility of the discharge should be made by inoculating a culture tube of serum agar. If no growth appears in forty-eight hours, the pus discharge is due to the tubercular process alone, and no further attempt to influence the local condition by means of vaccine need be made. The tuber-

culin treatment for the systemic condition, and bismuth paste for the local condition will suffice. If, however, the smear or the culture tube, or both, revealed the presence of mixed infection, we proceed to treat the patient with a stock vaccine after a diagnosis of the causative organisms is made. (See Chapter IV.)

Mixed infections in bone and joint disease are of the simplest forms.

The mixed infections occurring in tuberculosis of bones and joints are the simplest forms of infections for vaccine treatment. The causative organisms in the largest majority of cases are the staphylococcus, albus or aureus. The streptococcus comes next in order of frequency, occasionally the pneumococcus makes its appearance, and very rarely the colon. Thus it will be seen that the most easily distinguished bacteria, both in smear and culture,—the staphylococcus and the streptococcus—are responsible for most cases of mixed infection in bone and joint tuberculosis.

Stock vaccines may be employed. Autogenous vaccine should be resorted to when stock vaccine has failed.

A stock vaccine of one of the organisms found in the pus should be tried for a few weeks, the dosage being the same as for chronic mixed infections (Chapter IV). And if no effect is produced such as a change in consistency or in the quantity of the discharge, a stock vaccine of one of the other organisms should be tried for as long a time as the first. It may be necessary at times to obtain an autogenous vaccine to produce the desired effect. Especially is this true in the case of the streptococcus, where the strains are so numerous that the strain causing the infection may have been overlooked in the manufacture of the polyvalent stock vaccine.

Vaccines should be used singly.

As I have previously stated, it is better to use a vaccine of one organism at a time in case of multiple infection, than to use vaccines for all of the organisms at the same time. Not that there is any serious objection to the latter method, but since the tuberculin treatment must necessarily last a length of time which offers ample opportunity for the former or slower method of vaccine treatment, it should be adopted as it has distinct advantages. Thus it will often be found that when using a vaccine against one of the bac-

teria in a multiple infection, the other bacteria will disappear spontaneously, making it at once evident that they were simply parasitic forms and took no part in the mixed infection.

On the other hand, it may happen that after the use of a vaccine against one of the organisms, another may so increase in number as shown in a subsequent stained smear, that it leaves little doubt as to its participation in the infection. A vaccine for this organism should be at once employed. All these variations will become evident only if the vaccine therapy is applied in a spirit of scientific interest—the empirical use of vaccines will not only fail in a great many cases, but even when successful, will add nothing to the physician's experience which can be utilized in subsequent cases.

Chapter IX

BISMUTH PASTE

Bismuth paste is a prominent element in the COMBINED TREATMENT.

Having considered the treatment of the etiological infection and the treatment of the mixed infection of tubercular cavities and sinuses, we must now turn our attention to the reconstruction of tissues in order to remove the mechanism, which though it was established as part of the defensive processes of the individual, was so well established that the body cannot rid itself of it spontaneously once the reason for its existence has passed.

Formation of cavities and channels.

A better understanding of the mode of action of bismuth paste will be obtained if we have clearly before us the mechanism by which pathological cavities and sinuses form and continue their existence. In the first place nature builds a wall around a chronic infection as part of its protective mechanism. The products of the chronic infection must escape—hence the formation of sinuses and fistulas. Once the process is chronic, the necessity for the existence of the fistulous tracts will remain for a considerable length of time. Nature, therefore, lines these tracts in the same manner as she lines natural passages—with a secreting membrane. What was originally meant as protective construction, thus becomes the means of the prolongation of the pathological process. These cavities and sinuses are constantly filled with a sero-purulent irritating accumulation, aiding materially in prolonging their existence. The sero-purulent accumulation is brought about by the negative osmotic pressure, causing a flow of lymph and serum toward the empty space forming the cavity. This offers an admirable situation for mixed infections. The serous accumulation forms the best cultural media for bacterial growth—the proper temperature is always present, and the bacteria are at the same time beyond the reach of the antibodies.

Action of bismuth paste.

When such a cavity is filled with bismuth paste the following results are produced:

First, the bismuth paste possessing a specific gravity far in excess of the surrounding tissues, practically stops the irritating accumulations.

Second, mechanical pressure exerted by the bismuth paste upon the lining cells causes atrophy of these cells—thus removing one of the principal causes that prevent healing.

Third, bismuth acting as a foreign body stimulates the contraction of the tissues upon it so that the cavities hold less and less bismuth with each subsequent injection until final obliteration of the cavity takes place.

Fourth, according to Beck, bismuth possesses a kymotechtic property aiding in the production of hyperemia—the element that is most needed in overcoming chronic disease.

Fifth, bismuth paste possesses the quality of retaining to some degree radio-active properties, which are imparted to it by the X-rays. Frequent Roentgenographic examinations while the tubercular tract is filled with bismuth paste will facilitate the cure of these conditions.

Composition of Bismuth Paste

Bismuth paste consists of bismuth and vaseline. Hard paraffin and white wax is added when, owing to a large fistulous opening, it is difficult to retain, and a more solid consistency is required. The usual proportions are one-third bismuth, two-thirds vaseline. When five, ten or fifteen per cent. hard paraffin, together with five per cent. white wax are added, the bismuth content may be reduced to thirty per cent., and the vaseline quantum sufficit. The bismuth may be further reduced to twenty, ten or even five per cent., when the injection is made into a great depth, and where its removal may prove difficult, also where the cavity is of such size that the total quantity of bismuth paste injected

is large. I have seen lanolin used instead of vaseline. That is distinctly contraindicated, as lanolin is an absorbable base and would encourage the absorption of bismuth along with it. The use of lanolin as a base is probably responsible for the fear that bismuth paste may cause bismuth poisoning. In ten years of experience with bismuth paste, I have seen but one case where there seemed to be a tendency to bismuth poisoning, and that occurred in the case of pulmonary abscess, where fourteen fluid ounces of the paste had been injected in a patient for diagnostic X-ray examination. It was afterward discovered that this patient possessed a special idiosyncrasy for bismuth—the poisonous symptoms appearing after the injection of a very small quantity. Aside from this case, there never occurred the slightest suggestion of bismuth poisoning in the hundreds of cases that have come under my personal experience.

Bismuth Paste Formulas

Variations in the bismuth paste formula.

	I	II	III	IV
Bismuth Subnitrate	33 1-3	10	20	30
Paraffin (120 melting point)....				5
White Wax				5
Vaseline.....	66 2-3	90	80	60
	100	100	100	100

With regard to the therapeutic application of bismuth paste, the following are the most important points requiring attention:

Care and preparation for injection.

The bismuth paste must be absolutely smooth, as solid particles of bismuth may become separated from the vaseline and form a concretion. Only such quantity of the paste should be sterilized as is required for immediate use, for the frequent heating of the bismuth paste spoils the consistency of the vaseline and allows the precipitation of the bismuth. The sterilization of the bismuth paste for immediate use is accomplished: (1) by boiling a receptacle large

enough to contain the quantity of bismuth paste required, together with the syringe; (2) by putting the required amount of bismuth paste in the sterile receptacle which is then placed in boiling water. The flame under the boiling water is turned out, and the bismuth allowed to stand in the hot water for ten minutes. This permits of a pasteurization of the bismuth paste, the cooling of the water during the ten minutes not going below the pasteurization point. It is not necessary to boil bismuth paste to obtain sterility, as both bismuth and vaseline inhibit the growth of bacteria, hence pasteurization is sufficient to kill any bacteria that get in during the manufacture of bismuth paste.

The more fluid the paste, while being injected, the more certain it is to completely fill all the sinuses and cavities. However, care must be taken not to allow the paste to be hot enough to cause pain to the patient.

Bismuth Injections

A good syringe and gentle handling are the principal elements in the bismuth paste treatment.

The proper syringe is a plain glass syringe with an asbestos packing, the syringe varying in size from two drams to four ounces. It is best to have the tip blunt and rounded, as per illustration (Fig. 55), rather than a catheter end which would go into the fistula. I prefer to avoid putting into a fistulous tract any hard instrument which might cause injury and bleeding. The blunt point placed against the fistula's opening with gentle pressure will answer the purpose every time. Inject the bismuth slowly, using steady but gentle pressure until the patient feels discomfort from distension, or until the resistance causes an overflow of the paste around the tip of the syringe, or until the bismuth shows through the other fistula or fistulas.

Technic.

If more than two fistulas exist a gentle pressure is applied on the mouth of the fistula where the bismuth first makes its appearance, and the injection of the bismuth is continued until it begins to show at the mouth of the next fistula. The same pressure should be applied to the third fistulous open-

ing if a fourth exists. This procedure is continued until the bismuth appears from all the fistulous openings. Only then are we certain that if a cavity exists, it is filled with bismuth, and that all the accumulations in that cavity have been removed ahead of the advancing bismuth column.

If fistulas exist which do not communicate, bismuth should be injected into each separately.

Bismuth Paste Retention. Although bismuth paste is of value in removing the infective and irritative accumulations from fistulas and cavities, it cannot prevent reaccumulations nor stimulate contraction of the cavities unless it remains there for at least twenty-four hours, preferably forty-eight hours at a time. It is, therefore, necessary to prevent the immediate outflow of the bismuth paste after injection. That can be done in the first place by varying the consistency of the bismuth paste according to the size of the fistulous opening. For instance, a large opening must have thicker bismuth paste, whereas for a very small one a more fluid bismuth paste can be employed. In the second place, the consistency of the bismuth paste should depend upon the depth and the distance of the cavity from the surface. A cavity will retain bismuth paste of a lighter consistency for a sufficient length of time if the outlet to the surface is formed by a tortuous and long fistulous tract. Whereas a channel that is near the surface and has a short outlet will have to be filled with a bismuth paste that remains quite hard at body temperature. The consistency of the bismuth paste can be varied by the addition of five or ten per cent. hard paraffin (see formulas, page 219).

Varying consistency of bismuth paste for retention.

The fistulas can be sealed with cotton collodium or plugs of cotton or gauze, retained by adhesive plaster. Small tampons may be used, pushed into the channel and prevented from falling beyond reach by an attached string which is tied over an adhesive strip going across the opening; or a string attached to a piece of adhesive plaster may be placed at opposite sides of the fistula and at some distance from it.

By tying these strings together, the adhesive plasters are drawn together, pulling the skin with them, thus closing the fistula.

Intervals between injections, and instruction to patients as to the care of the dressing during the intervals.

Frequency of Treatment. The best interval between injections is forty-eight hours. If the bismuth is well retained, the intervals may be longer. However, the interval should not be longer than a week. It is best to renew the bismuth paste in the diseased area at least once a week for two reasons: (1) to prevent the formation of concretions; (2) to avoid unfavorable results that may occur in a fistulous branch which may not have been filled by the bismuth, and which retains its irritating and infective contents as a result of the blocking of the exit by the bismuth. In case redressing of the fistulous opening by the patient becomes necessary during the interval, the patient is instructed always to use gauze or cotton saturated in alcohol, to avoid the constant danger of reinfection.

Where there is only one fistulous opening, making it therefore impossible to remove the old bismuth ahead of the advancing column of the fresh bismuth, and where the bismuth does not spontaneously ooze out during the interval, we follow the advice of Beck by using injections of sterile olive oil to soften and wash out the bismuth just previous to the injection of the fresh paste.

The Proper Direction of Bismuth Paste

Adequate counter openings must be present to allow of the escape of the purulent contents ahead of the advancing bismuth column.

A closer study of a number of cases of open bone disease that resisted the *combined treatment,* has yielded a more intimate understanding of the mechanism which continues the existence of cavities, sinuses and fistulas. Aside from the well known purpose for the existence of fistulas and sinuses —drainage,—the study revealed the importance of a proper direction for such drainage in relation to bismuth paste injection. This finding at once explained that the former resistance to treatment in many cases was due to a faulty direction of the flow of the bismuth paste. No sooner was

this direction altered in such a way as to conform with the principles of bismuth paste injections, than conditions which resisted treatment for a number of years promptly began to improve and soon healed.

In the process of formation of fistulous tracts the area through which the inflammatory products have to traverse in order to reach the surface may be composed of such tissues that in taking the direction of least resistance, the course becomes zigzag and tortuous. For instance, when heavy fascial layers interpose between the point of bone infection and the surface of the body, the direction of drainage may be deflected by this fascia for a varying distance, allowing it to come to the surface where the fascial layer either thins or disappears. The fistulous opening, therefore, will appear at a point removed from the point of bone infection—in fact, at times the distance is so great that only special investigation will discover the relation between that fistulous opening and a given bone infection.

In other cases the suppurative process takes two or more directions before reaching the surface. But not all such fistulous tracts need reach the surface. For, as soon as one or two of the tracts do reach the surface, the pressure is relieved and the process in the rest of the sinuses discontinues. The result is the formation of blind fistulas or pouches.

Counter openings must often be established surgically.

It is difficult to fill completely blind fistulas and pouches which are really cavities, having only one opening at some distance from the cavity itself. Where several counter openings exist through which the bismuth can escape, it is almost impossible to fill such blind fistulous pouches. The advancing bismuth column turns the corner and leaves through a neighboring sinus, and thus not only fails to completely fill, but even bottles up the discharge in the blind fistula or pouch. This circumstance is responsible for the sudden pointing of a new abscess and the formation of an added fistula during treatment. For the moment such an occurrence is discouraging and is looked upon as evidence of fail-

ure, and frequently leads to the discontinuance of the treatment. In truth nature has accomplished something which the physician should have done long before—established the proper direction for the passage of the bismuth paste. A reference to the diagram (Fig. 50) will render this subject clearer.

Roentgenography

Without the aid of the X-ray photograph the necessity for counter-openings cannot be discovered.

The direction of the bismuth paste cannot be determined without one or two X-ray examinations made during treatment, and so some mention of the utility of Roentgenography in this connection should be made. It is almost impossible to gain any knowledge of the various channels or cavities—whether as to size or direction—without an X-ray photograph of the entire part involved completely filled with bismuth paste. Probing is to be condemned even if it were to enable the determination of anything of diagnostic value. A glance at Fig. 51 will show how hopeless the probing would be in such a network of channels.

The stereo X-ray is best.

The stereoscopic radiograph is the latest development of X-ray study. By taking two exposures of the same part on separate plates, each exposure from a different angle and the difference gauged to correspond to the difference in the angles between the human eyes, a stereopticon picture is produced which when viewed through a stereoscope shows the part in three dimensions. The exact relations of the various tubercular channels and cavities to the tissues are seen, which render the application of the various surgical measures far more easy. If possible, a stereo-radiograph should be insisted on.

Therapeutic X-ray applications.

The X-ray has another important application in relation to bismuth paste—that is a therapeutic application. It was noticed that those cases that were exposed to the X-rays after bismuth injection for diagnostic purposes healed more rapidly than those cases that were treated with bismuth paste but never had an X-ray photograph taken. This led

EXPLANATION OF FIG. 50

When bismuth paste is injected at F2 it will go in the direction of least resistance and escape at F1. If F1 be closed by a dressing sufficient to prevent the escape of the bismuth, the paste will then rise until it reaches b, where the branch sinus d is given off. Then instead of rising to fill the blind sinus a, and the cavity c, it takes the direction down through d because that is the direction of least resistance communicating as d does with the surface through the fistulous openings F3, F4, F5, F6, F7, and F8. Whereas, in attempting to fill a and c, the paste would have to replace an amount of discharge which has no outlet once the point b is filled. In this case, a puncture incision, after a little cocaine infiltration, at X which was nearest the surface, removed the only barrier to a cure. Subsequent bismuth injections were given through this puncture at X, which permitted of an easy filling of the entire system of fistulas and cavities.

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EXPLANATION OF FIG. 50

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FIG. 50.

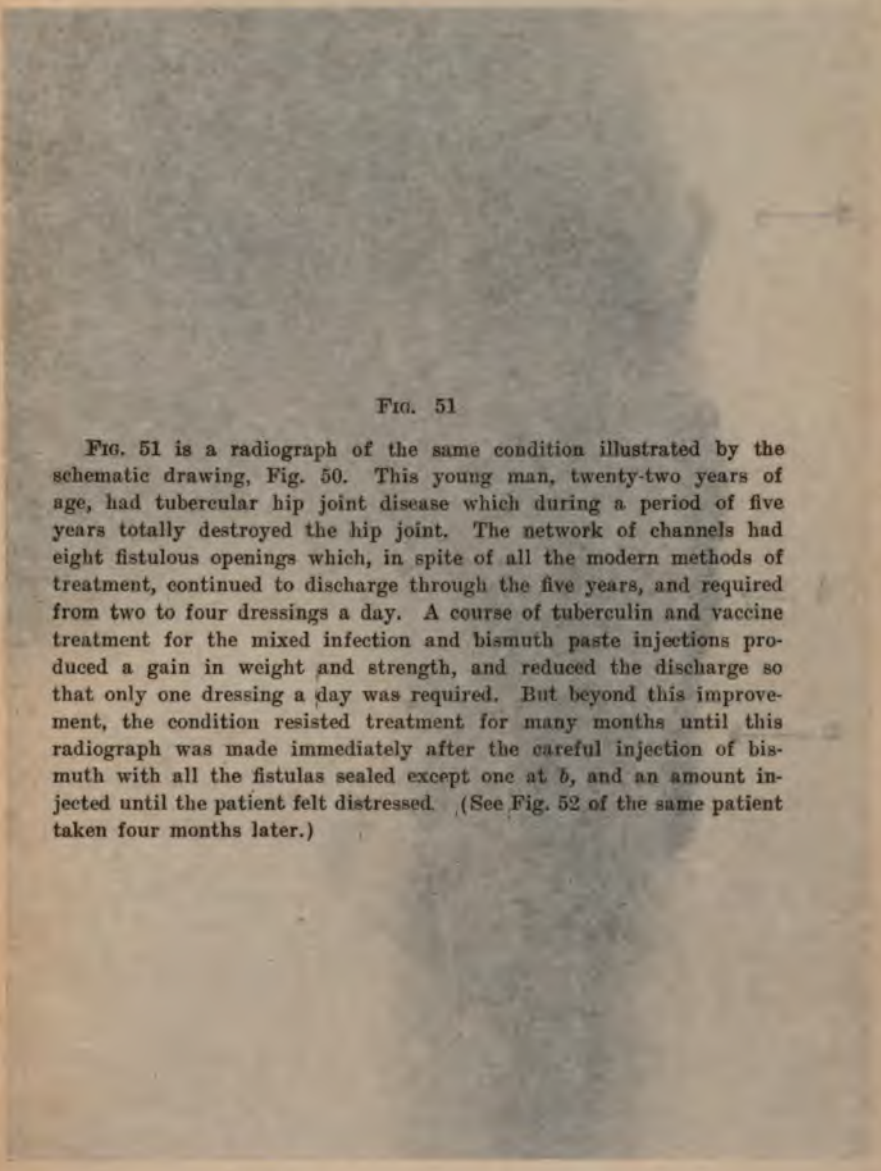

FIG. 51

FIG. 51 is a radiograph of the same condition illustrated by the schematic drawing, Fig. 50. This young man, twenty-two years of age, had tubercular hip joint disease which during a period of five years totally destroyed the hip joint. The network of channels had eight fistulous openings which, in spite of all the modern methods of treatment, continued to discharge through the five years, and required from two to four dressings a day. A course of tuberculin and vaccine treatment for the mixed infection and bismuth paste injections produced a gain in weight and strength, and reduced the discharge so that only one dressing a day was required. But beyond this improvement, the condition resisted treatment for many months until this radiograph was made immediately after the careful injection of bismuth with all the fistulas sealed except one at *b*, and an amount injected until the patient felt distressed. (See Fig. 52 of the same patient taken four months later.)

FIG. 51.—DIRECTION OF BISMUTH PASTE.

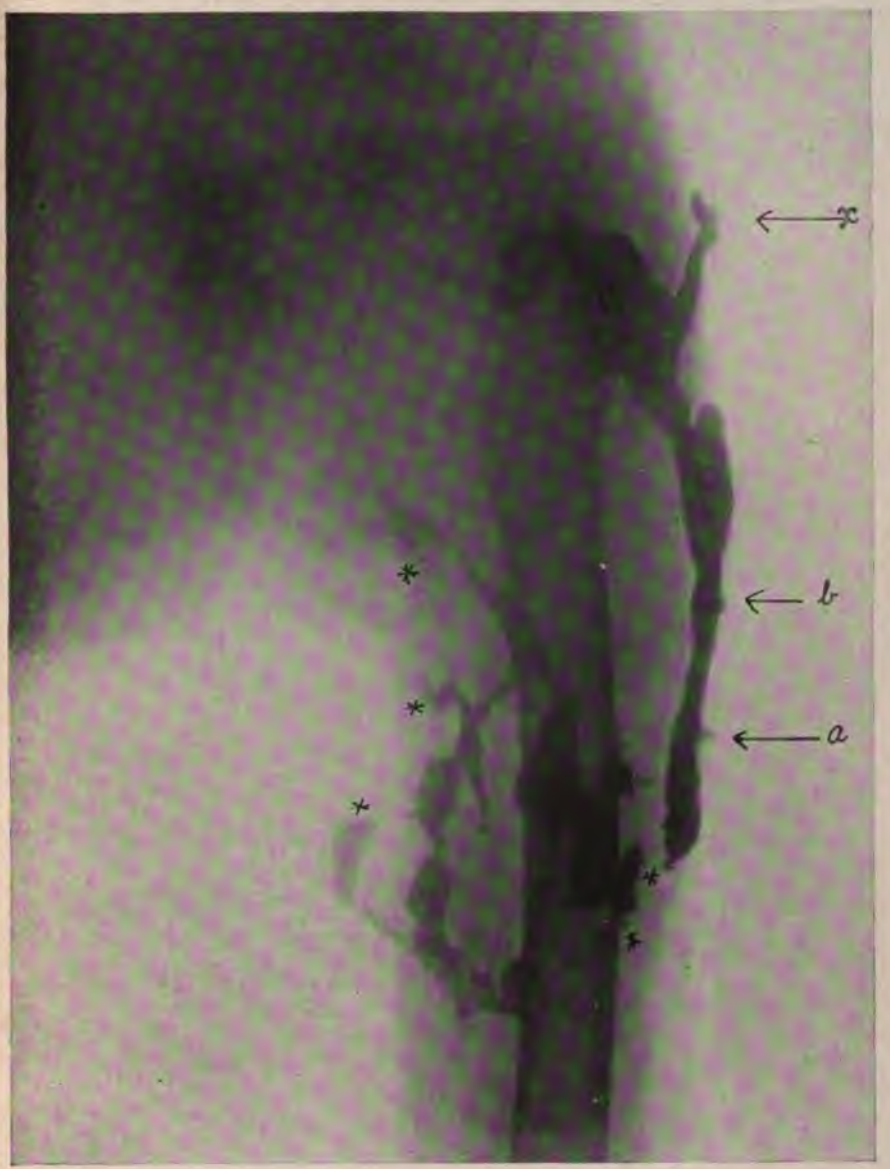

FIG. 51.—DIRECTION OF BISMUTH PASTE.

FIG. 52

FIG. 52 is a radiograph of the same patient as Fig. 51 four months later. The entire condition is healed except for the fistulous opening at *b*, which admitted a few drops of bismuth paste. Traces of bismuth may still be seen in the tissues around the hip joint and on the inner side of the leg below.

It is nearly a year since this radiograph was made and no recurrence has taken place. The patient is now employed and self-supporting.

FIG. 32

FIG. 32 is a radiograph of the same patient as Fig. 31 four months later. The entire condition is healed except for the fistulous opening at L, which admitted a few drops of bismuth paste. Traces of bismuth may still be seen in the tissues around the hip joint and on the inner side of the leg below.

It is nearly a year since this radiograph was made and no recurrence has taken place. The patient is now employed and self-supporting.

FIG. 52.—DIRECTION OF BISMUTH PASTE.

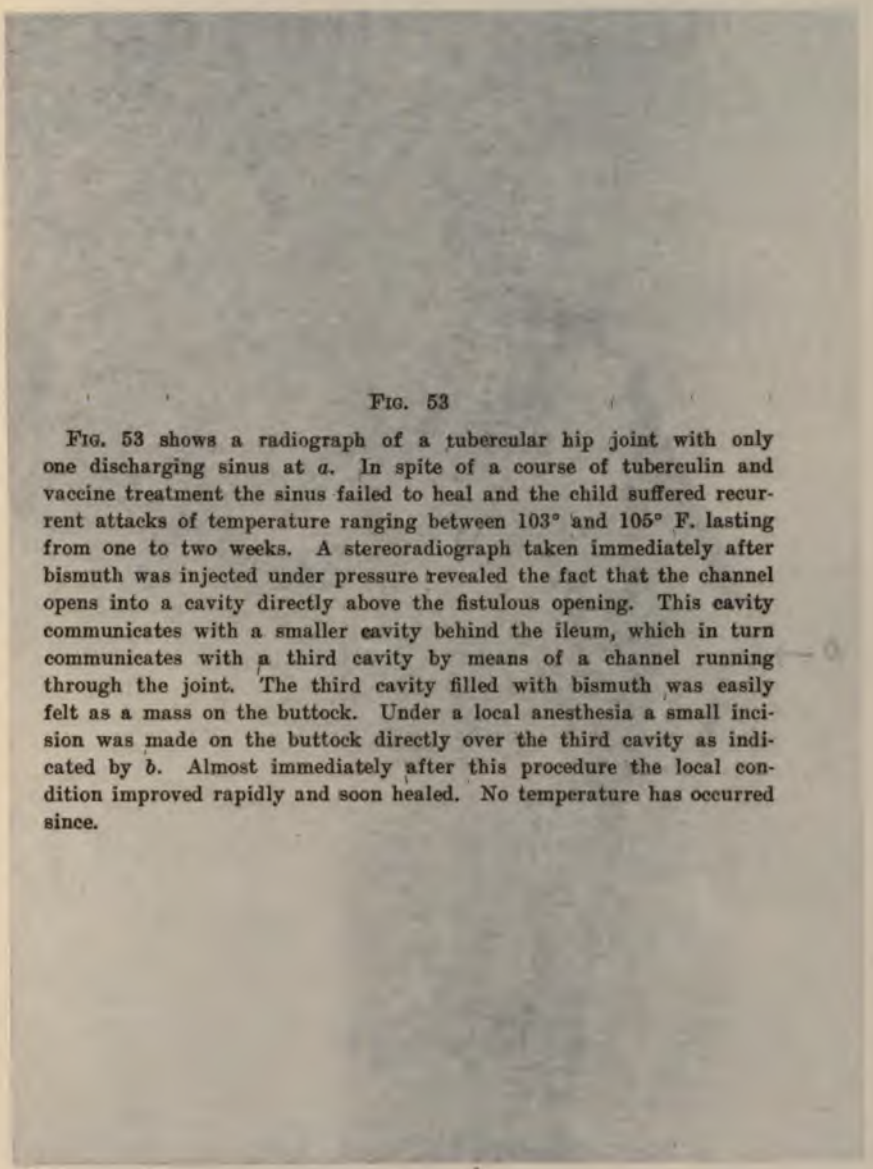

FIG. 53

FIG. 53 shows a radiograph of a tubercular hip joint with only one discharging sinus at *a*. In spite of a course of tuberculin and vaccine treatment the sinus failed to heal and the child suffered recurrent attacks of temperature ranging between 103° and 105° F. lasting from one to two weeks. A stereoradiograph taken immediately after bismuth was injected under pressure revealed the fact that the channel opens into a cavity directly above the fistulous opening. This cavity communicates with a smaller cavity behind the ileum, which in turn communicates with a third cavity by means of a channel running through the joint. The third cavity filled with bismuth was easily felt as a mass on the buttock. Under a local anesthesia a small incision was made on the buttock directly over the third cavity as indicated by *b*. Almost immediately after this procedure the local condition improved rapidly and soon healed. No temperature has occurred since.

FIG. 53

FIG. 53 shows a radiograph of a tubercular hip joint with only one discharging sinus at a. In spite of a course of tuberculin and vaccine treatment the sinus failed to heal and the child suffered recurrent attacks of temperature ranging between 103° and 105° F. lasting from one to two weeks. A stereoradiograph taken immediately after bismuth was injected under pressure revealed the fact that the channel opens into a cavity directly above the fistulous opening. This cavity communicates with a smaller cavity behind the ilium, which in turn communicates with a third cavity by means of a channel running through the joint. The third cavity filled with bismuth was easily felt as a mass on the buttock. Under a local anæsthesia a small incision was made on the buttock directly over the third cavity as indicated by b. Almost immediately after this procedure the local condition improved rapidly and soon healed. No temperature has occurred since.

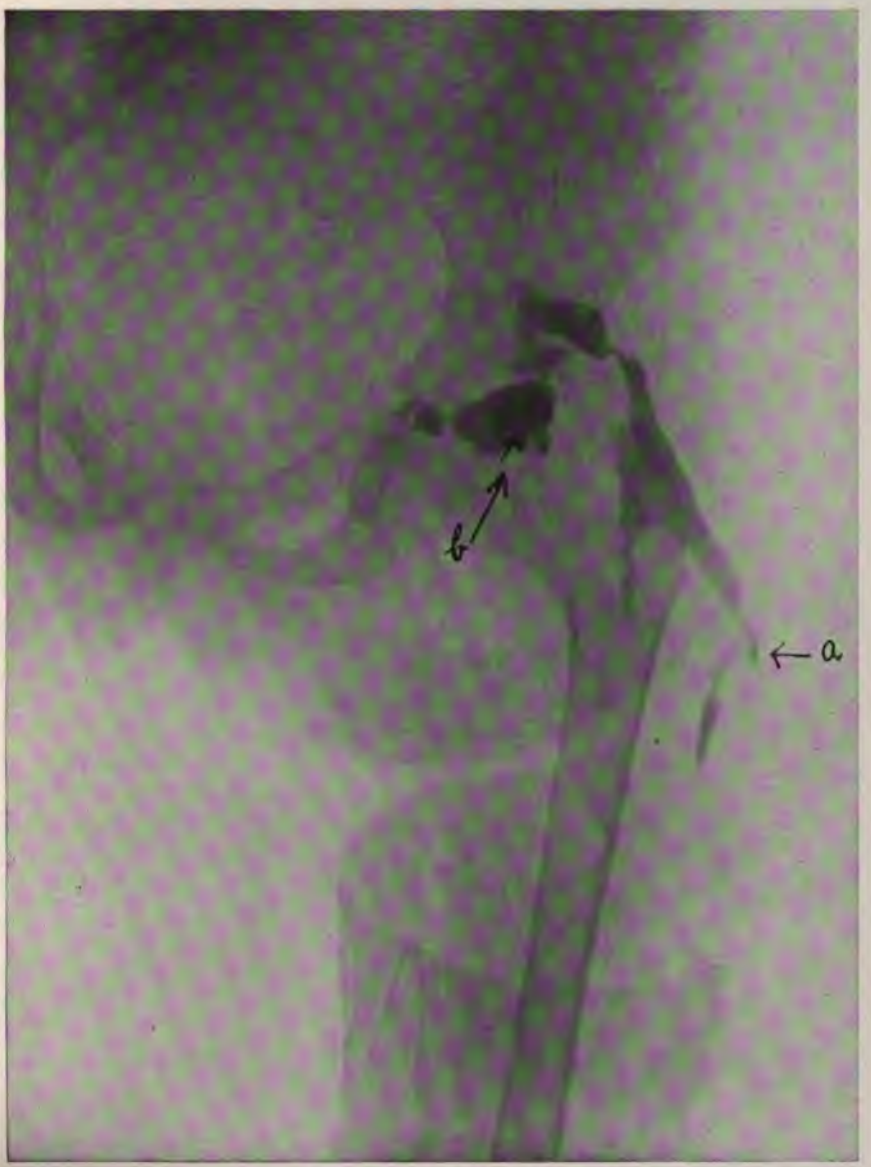

FIG. 53.—DIRECTION OF BISMUTH PASTE.

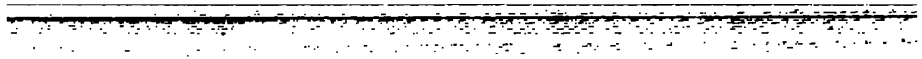

FIG. 54.—DIRECTION OF BISMUTH PASTE.

FIG. 54 is a photograph of the same hip as radiograph, Fig. 53, with a schematic outline of the tuberculous tract, the solid area showing the anterior and the ruled area the posterior part of the tract. The heavy dot represents the fistulous opening artificially made.

FIG. 55

A young man twenty-two years old, with a negative family history, had nothing in his past history that had any bearing on his present complaint, except that he had had measles and scarlet fever. His present complaint began five years ago with the formation of an ischiorectal abscess which refused to heal and was operated upon for fistula-inano. The fistula, however, recurred and persisted for several years. A second extensive operation with no better results was performed a year before he came to me for treatment. The usual routine as to tuberculin, vaccine, and bismuth paste was carried out. But in spite of increased weight and strength, and in spite of the fact that he was able to return to full duty at his occupation (which he had not been able to do for years), the local condition did not completely heal. There was only one large fistulous opening into which about three drams of bismuth paste could be injected, but the fistula was still there at the conclusion of the tuberculin treatment. After careful radiographic study one fistula was found to lead to the sacrum. A puncture incision was made at that point and the bismuth paste injected at the new opening until it appeared at the old opening as shown in this photograph. In less than two weeks the discharge stopped. The local condition improved more in the next two weeks than it had in the six months of previous treatment.

FIG. 55.—TUBERCULAR COXITIS—DIRECTION OF BISMUTH PASTE.

to periodic exposure of the more refractory cases that were treated with bismuth paste to the therapeutic X-rays. The results thus obtained are sufficient to recommend the occasional exposure of the bismuth filled tubercular channels to the X-rays.

Chapter X

COLD ABSCESSES

A cold abscess is a pathological condition which requires treatment.

It has become a matter of principle among the profession to ignore cold abscesses entirely. Whether this attitude arose from fear of mixed infection, or from the desire to leave well enough alone, is hard to tell. Perhaps the bad results obtained from wide incisions and drainage has led to the usual reaction—from doing too much to the opposite of doing too little or nothing at all.

Infection through aspiration is rare.

Personally I could never see the harm in emptying a cold abscess. As a result of the surgical treatment of a cold abscess, the following three possibilities may arise: infection may take place; the abscess may refill; or the abscess may remain empty, the capsule contracting into a small mass of connective tissue.

With aseptic technic developed to its present standard, the mixed infection need not form such an impassable barrier to the proper treatment of a cold abscess, especially as the methods used in emptying a cold abscess here described, almost entirely eliminate the danger of infection. We do not make wide incisions, nor do we use drainage tubes, nor packing such as is done in inflammatory abscesses of equal size.

The purpose of aspiration is to forestall the tryptic digestion and inflammation which irritation will produce.

The refilling of the abscess is of no greater consequence than the recurrence of effusion in pleurisy. It entails no greater danger than the necessity for re-emptying. However, at the present time, we even can to a large measure prevent the refilling of the abscess.

Now, "Why get rid of the cold abscess?" is the question. The first and foremost reason is that a cold abscess is a pathological entity and will take away the psychological effect of the benefit from tuberculin if it fails to absorb during the healing of the other tubercular lesions. Secondly, these abscesses are usually on the surface of the

body, and may become infected through the pressure of clothing or through outside trauma far more frequently than through the use of an aspirating needle which is always used with strict asepsis. In the third place, the abscess frequently breaks down through a tryptic digestion which may make its appearance at any time. This tryptic digestion is the method by which Nature rids herself of foreign matter when there is no pyogenic organism present. This digestion usually attacks the entire surface of the skin over the whole abscess and produces a proportional amount of very sluggish ulcerations with eventual irregular scarring.

A staphylococcus infection is almost preferable in a cold abscess to this digestive breakdown, because the former will point in but one place and an incision followed by drainage will localize the infection, which on healing leaves an insignificant scar. In the latter case, the abscess empties by a sloughing process through the tissues, leaving behind the most unsightly scars.

Treatment

Treatment consists mainly of aspiration and the injection of bismuth paste or olive oil.

The best treatment for cold abscesses is aspiration. An ordinary aspirating needle about the size used for obtaining spinal fluid is best. A drop of tincture of iodine painted on the skin over the dependent part of the abscess, and a little ethyl chlorid spray for local anesthesia, is all the preparation that is necessary. The needle is pushed into the abscess, care being taken not to push it too suddenly and thus injure the opposite abscess wall and produce bleeding into the abscess cavity. All the fluid is aspirated and sterile oblive oil injected through the same needle, filling the cavity to the extent of about one quarter of the amount aspirated. Frequently the needle tract will fail to heal and will form a small fistula through which any reaccumulation will slowly ooze until the capsule entirely contracts.

Another form of treatment is by puncture. After paint-

In a very large abscess a fistulous opening should be established by puncture and then the abscess treated with bismuth paste injections.

ing the skin with tincture of iodine, a drop of one quarter of one per cent. of cocaine is injected at the point where the puncture is to be made. The same knife is used as in the puncture of soft glands (page 209), then the abscess is emptied by gentle pressure and refilled with sterile olive oil. The bismuth paste syringe, or an ordinary medicine dropper may be used for injecting the sterile olive oil. The amount of oil injected should be about one quarter of the amount of matter withdrawn, or a quantity sufficient to keep the opposite walls of the cavity from touching, as any irritation will hasten a reaccumulation of pus in the abscess cavity.

When puncture is resorted to instead of aspiration, and when the abscess is not very large, bismuth paste may be injected after emptying. Bismuth often hastens the contraction of the capsule, and a rapid disappearance of the abscess occurs as a result. The same may occur after aspiration. A precipitate which forms in the fluid content of the cold abscess forms a pseudo-lining to the capsule. The capsule remaining after the aspiration of the fluid, with a solid substance within it, promptly contracts, forming a nodule which may protrude from the surface of the skin. The nodule dries and falls off after a few days, leaving a smooth circular scar behind.

When the cold abscess is very large, or when it resisted the above treatment, a more radical procedure is resorted to (in fact the most radical we ever need use) consisting of an incision, never more than one-fourth to one-half an inch long, and followed by drainage. As a drain, a few strands of silk or a very narrow strip of rubber tissue is used. In forty-eight hours we have established a fistula and now can treat the cold abscess as we treat bone cavities. Bismuth paste is injected every forty-eight hours, care being taken to remove first any bismuth paste which has not oozed out from the previous injection. Even a thirty per cent. bismuth paste may be used here.

Gauze packing or drainage by means of a rubber tube or gauze should be avoided.

Under no circumstances should a cold abscess be packed with gauze, nor should drainage with rubber tubing or gauze ever be resorted to. The danger of infection is far less when the cold abscess is left without drainage altogether. We may reduce the danger of infection still further by means of an alcohol compress applied to the incision after each treatment, and by means of scrupulous care in sterilizing the syringe and the bismuth before use. I have had no serious trouble with infections in treating cold abscesses in the manner just described, although I have opened a great many over a period of eight years.

It is far better, however, to leave cold abscesses entirely alone, than to treat them improperly. The following case is an example of the serious harm that can be done by the application of the usual surgical principles to cold abscesses:

Example.

The patient, a man twenty-one years of age, with an old tubercular lesion in the dorsal spine, developed a large cold abscess occupying the entire posterior surface of the left thigh. Without any special indication for surgical interference, an operation was decided upon. The patient was taken to a hospital and under ether anesthesia, a two-inch incision was made at the upper end of the abscess, another at the lower end, and a rubber tube pulled through and left protruding from both incisions, in order to insure perfect drainage. The patient had no temperature, and I believe the lesion in his spine was not active. Three days after the operation, the patient developed a temperature of 105.5° F. with a typical streptococcus septicemia. After the infection persisted for a week or over, the patient's condition became alarming, and I was called in to institute vaccine treatment. An immediate removal of the rubber tube and a thorough washing out of the cavity with alcohol, together with the use of a streptococcus vaccine, soon placed the infection under control. In a week, normal temperature was again restored. I am quite certain that had one or two punctures been made for the escape of the fluid, followed

by the injection of a bland, oily substance to prevent the rubbing of the opposite walls, the abscess could have been healed without any trouble.

I might add here, that, owing to the size of the abscess (it held nearly a pint of fluid), it would have been against the best interest of the patient to have omitted treatment altogether, although no treatment would have been better than what the patient first received. When the digestive process sets in, the sloughing of the skin over the abscess is so extensive that great discomfort, lasting for months on account of the slow healing ulcerations, is produced.

Chapter XI

EMPYEMA AND LUNG ABSCESS

Purulent effusion in the pleural cavity is a complication in tuberculosis that occurs in four different ways:

(1) Infection of serous effusion;

(2) The pointing and breaking of a pulmonary abscess into the pleural cavity;

(3) The ulceration of a pulmonary cavity and its opening into the pleural cavity;

(4) The infection of the pleural cavity by the extension of a mixed infection from tuberculosis of the ribs or spine.

A lung abscess complicating phthisis may communicate with a large bronchus and drain by means of cough and expectoration; it may communicate with the pleural cavity; and it may communicate with both with the bronchus and the pleural cavity.

The bacteriology of empyema and lung abscess is apt to be very complicated unless treatment is applied early when the bacteria concerned in the etiology of the infection decidedly predominate and are easily recognized. The following are the bacteria which are mainly concerned in these processes:

Streptococcus
Pneumococcus
M. catarrhalis
M. tetragenus
B. Friedlander
B. coli
B. proteus
Staphylococcus
B. pyocyeneus
B. influenza

Treatment

Treatment consists of three distinct measures which should be applied together ("combined") as each has its distinct indication. As is true in all forms of tuberculosis, treatment can only be effective in the largest number of cases when the *combined methods* are used. These methods are:

Vaccines against the infection;

Modified surgical measures for drainage or for the removal of purulent materials;

Treatment of the condition for the prevention of reaccumulation of purulent material and for the stimulation of the healing process.

Vaccines Against the Infection. The vaccine treatment of purulent effusions or pulmonary abscesses is the same as the vaccine treatment in acute pulmonary mixed infections both as to dosage and intervals (see page 193). However, the local treatment of the condition is far more important than the vaccine treatment. The purulent accumulation is so large in quantity that the bacterial growth can take place in spite of a sufficient immune response. The bacterial growth occurs beyond the reach of the defensive substances of the individual. When the antibodies do enter into the large effusions they become so diluted that only a small proportion of the invading organisms are reached.

Modified Surgical Measures for Drainage or for the Removal of Purulent Materials. Although drainage is of primary importance in the treatment of both purulent effusions and pulmonary abscesses it is unnecessary to resort to radical surgical measures such as are employed where surgery is the only measure instituted for the relief of the condition. Through the application of the combined measures for controlling the infection, the removal of the purulent accumulation and the prevention of reaccumulation, the surgical measures can be greatly modified. It is sufficient to make a half inch incision under cocain or novocain anes-

thesia in an intercostal space for the passage of a medium sized catheter through which the purulent effusion may be aspirated, using for this purpose either a syringe or vacuum suction. Through the same catheter, warm sterile normal saline should be injected several times and again aspirated in order to wash out the abscess or pleural cavity. This procedure should be repeated daily until the fluid withdrawn is no longer purulent.

Local Treatment for the Prevention of Reaccumulation of the Purulent Materials and for the Stimulation of the Healing Process. After the abscess or pleural cavity is emptied and washed of purulent material, sterile olive oil should be injected and left in the cavity until the next treatment. The quantity of olive oil injected should be about one-half of the amount of purulent fluid withdrawn, except in cases where the pulmonary abscess communicates with the bronchus. In that case the olive oil should be injected until coughed up through the mouth. The distress and vomiting produced by the foul discharge coming up through the bronchus almost entirely disappears after the injection of olive oil. In cases of purulent pleurisy and in cases of pulmonary abscess where the communication with the bronchus still exists, vaccines, cleansing, and olive oil injections are sufficient. In case of a pulmonary abscess which becomes adherent to the parietal pleura and communicates directly with the surface of the body, and where the communication with the bronchus has healed over or never existed, bismuth paste should be employed. Beginning with Formula 1 bismuth paste (page 219) the subsequent injections should be made with the stronger formulas if no tendency of bismuth poisoning has appeared. By means of olive oil injections the bismuth can be easily washed out in case of poisoning.

In the following three illustrations will be found typical examples of each of the three different forms of pulmonary abscesses: one communicating with the pleura and produc-

ing a purulent pleurisy: one communicating with the bronchus allowing of vaccine treatment only; one communicating with both the pleura and bronchus. I have added a fourth illustration to emphasize the necessity of radiography for the diagnosis of these conditions. This patient was pronounced hopeless on account of a pulmonary abscess and purulent effusion, whereas the radiograph disclosed the existence of an extra pleural pus cavity leading above to the diseased vertebra and running down to the pelvis.

FIG. 56

A young woman twenty-four years old had pulmonary tuberculosis for four years, and in spite of change of climate, hygienic and dietetic treatment, the disease progressed until there was involvement of the apex of the right lung and of the entire left lung with a cavity in the middle of the left lung. Two years ago she was brought to me for tuberculin and vaccine treatment. On examination her case seemed hopeless, but fearing that my refusal of treatment would disclose the hopelessness of the condition to the patient and thus hasten her death, her relatives requested me to treat her with tuberculin irrespective of my prognosis. My fear was that the three trips a week to my office in order to get the treatment would overtax the strength of the patient in her already weakened condition. However, the renewed hope for cure, together with a marked response to the tuberculin treatment had a wonderful effect on the patient.

After a year and a half of the treatment she had gained in weight, was much stronger so that she was able to attend to all her household duties. She still had a morning cough productive of sputum, but the amount of sputum was greatly diminished and the tubercle bacilli had disappeared entirely five months after beginning the treatment. The X-ray findings at this time showed the right lung greatly enlarged through emphysema, the left lung greatly contracted and the cavity, though still present, somewhat smaller. After the conclusion of tuberculin treatment, and contrary to instruction, she did not return at the end of three months for the test for the return of hypersusceptibility, and for the examination of sputum for determining the renewal of the vaccine treatment. Six months later I was called to her home and found that she had had an attack of grippe and for seven weeks had a daily temperature rise to 103° or 105° F. The doctor in attendance had pronounced her condition hopeless for he could hear no breathing sounds in the left lung and considered it a case of tubercular pneumonia. As three weeks had passed and the patient was still in the same condition, I was called in for consultation. The first glance at the patient was sufficient to discover that the left pleural cavity w

FIG. 56.—Pulmonary abscess draining into the pleura and producing an empyema.

menciously distended with fluid. Examination showed that her heart pushed to the right, and the chest which had been retracted on the left side was now decidedly bulging. An aspirating needle brought out a very thick foul smelling pus. Owing to the cyanotic and dyspneic condition of the patient, I decided to drain the pleural cavity at once. After cocain infiltration, a stab incision was made in the seventh interspace on the left side of her back. Ninety-eight ounces of pus were withdrawn, and through a soft rubber catheter one quart of sterile olive oil was injected. For the next ten days the pleural cavity was emptied through this catheter, washed out with normal saline and refilled with a constantly decreasing amount of sterile olive oil. At no time was a drain of any kind left in the incision. Two days after the incision was made the temperature dropped to normal and remained there.

The above radiograph was taken one month after the discontinuation of all local treatment of the abscess. It corroborated the earlier conclusion that the cavity had ulcerated through and broken into the pleural cavity, that the lung had become adherent to the pleura after the pus had been withdrawn, and that the lung cavity is in direct communication with the external fistulous opening. The bismuth paste which was injected for this X-ray photograph entered directly into the lung abscess.

An important point which this case brings out is the fact that the communication between the original lung cavity and the bronchus healed across immediately after the drainage of the pleural cavity. The cough and expectoration which persisted after the tuberculin and vaccine treatment now disappeared. The patient declares that she is better than she has ever been since the beginning of her illness. The most prominent bacteria found in the pus of the pulmonary abscess, and for which vaccines were made were the streptococcus, m. catarrhalis and the pyocyaneus.

FIG. 57.

Over a period of four years this patient had repeated attacks "pneumonia" lasting from one to three weeks, and characterized bloody sputum, high temperature and dyspnea. Each attack left hi with a severe cough which was productive of a large amount of fo smelling expectoration, and which lasted for varying lengths of tim Every time the cough ceased there would be a fresh attack of "pne monia." The fifth attack was accompanied by an unusual amount blood in the expectoration leading to the diagnosis of tuberculosis a the reference of the case to me. The nature of the patient's temper ture curve was typical of pyemia. His temperature ranged fro normal in the morning to 103° and 105° F. in the afternoon. The was distinct dullness over the middle right lung, and it had be noticed that all the pneumonic processes always localized in the sam place and never spread beyond it. This temperature curve, the patient history, and character of his sputum led to the diagnosis of lun abscess draining through a bronchus. The X-ray confirmed th diagnosis.

An autogenous vaccine was made of the streptococcus and pneum coccus found in the sputum, and after the first dose of forty millio streptococcus and twenty-five million pneumococcus, the temperatu came down to normal. Although it may be claimed that the temper ture came down after the establishment of proper drainage throug the bronchus, as in previous attacks, it cannot be denied that th complete healing was brought about by the vaccine. That the patien is cured is evidenced by a gain of over twenty-five pounds in weigh the disappearance of the cough and expectoration soon after the tem perature was reduced to normal. Although there was no recurrence o "pneumonia" for over a year, a course of tuberculin treatment wa also administered as the original cause of the abscess was no doub tubercular in nature. During the tuberculin treatment the tubercula process in the apex of the right lung and in the upper half of the lef lung cleared up.

The above radiograph was taken after the expectoration becam profuse and the abscess had more or less emptied. The abscess woul show more distinctly if the radiograph had been taken two days earlie

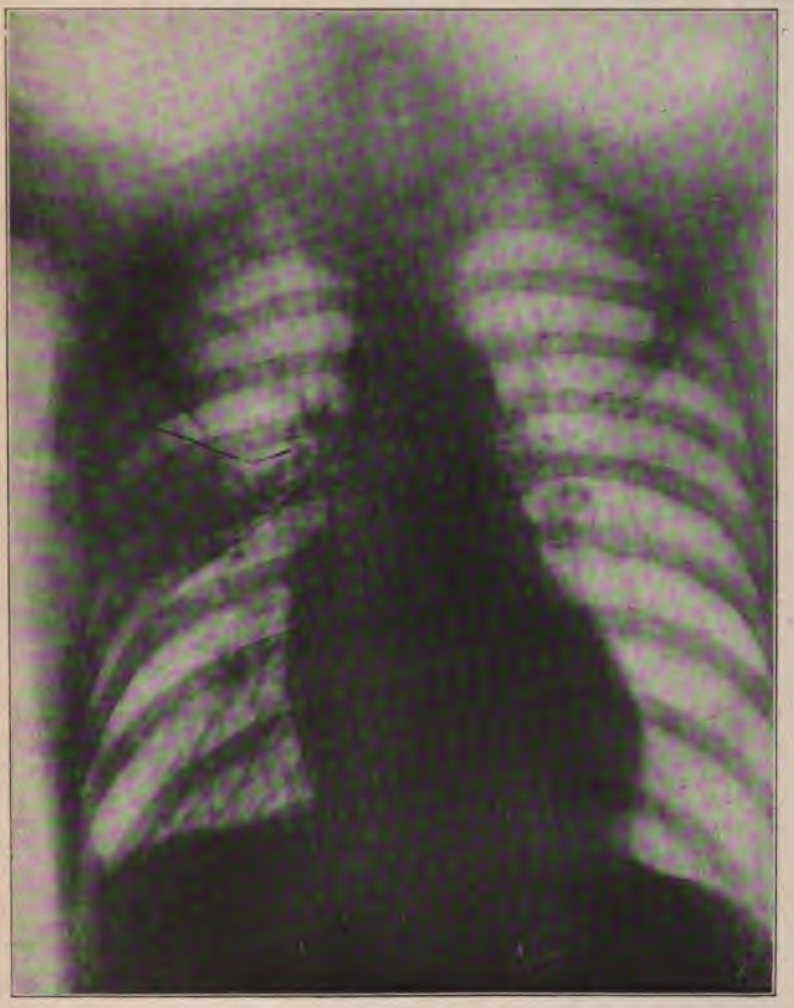

FIG. 57.—Pulmonary abscess draining into a bronchus.

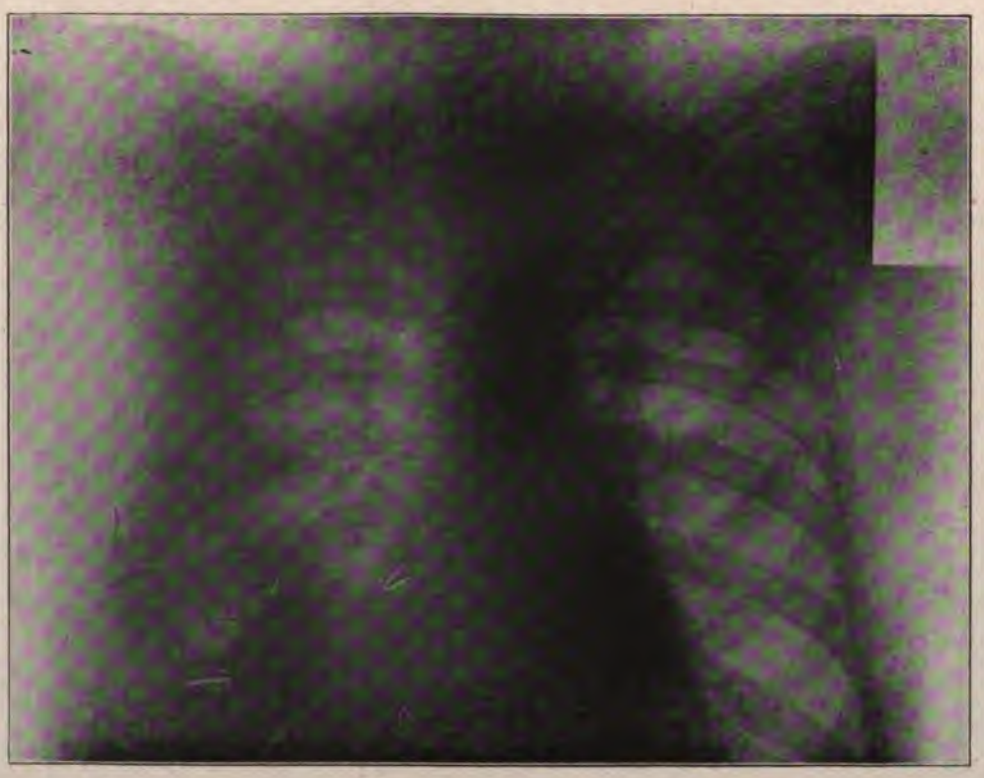

Fig. 58.—Pulmonary abscess draining into a bronchus and into the pleura.

FIG. 58.

During a mild tubercular lesion in the apex of the right lung the patient suffered an attack of lobar pneumonia involving the entire right lung. This attack terminated by lysis and finally developed into a typical case of unresolved pneumonia which after six weeks was finally recognized as a pulmonary abscess. The temperature at this time was of the septic type rising daily to 104° and 105° F. with marked dyspnea. An Estlander operation was immediately advised but the patient's family refused on account of the bad prognosis rendered by a number of physicians. When I first saw the patient he was in the most desperate condition, cyanosis and dyspnea were marked. He was greatly emaciated not only on account of his disease but on account of his inability to partake of any kind of food. His expectoration was so copious and so foul smelling that it would bring about gagging and vomiting after any attempt at swallowing. He presented such a poor subject for a radical operation, that I had no hesitancy about offering as good a prognosis with conservative treatment. At the New York Polyclinic Hospital I made a one-half inch incision under local anesthesia in the sixth intercostal space two and a half inches to the right of the spine. The foul smell of the discharge which drained through this incision drove all the attendants out of the operating room. The predominant organisms were the streptococcus and pneumococcus. An autogenous vaccine was immediately made. In spite of daily cleansing and profuse drainage through the incision the patient continued to bring up large quantities of pus. After three or four inoculations with the autogenous vaccine, however, the discharge changed and became mucoid instead of purulent. A smear made of the pus at this time showed none of the offending organisms. The temperature came down to normal. After five weeks in the hospital the patient was able to leave and to come to my office for treatment of the local condition of the abscess. Bismuth paste treatment was not thought advisable, but after the injection of a ten per cent. bismuth paste for diagnostic purpose, distinct bismuth poisoning appeared (one of the only two cases of bismuth poisoning I have ever seen). Owing to the discovery of the lead line at the gingival margins of the teeth, olive oil was used in order to wash out the bismuth paste. Several ounces of the olive oil were injected through the incision and then aspirated with the bismuth paste. This was repeated two or three times until the aspirated oil showed no further trace of bismuth, and to make certain, olive oil was injected and left in the abscess cavity to drain out slowly in order to carry with it any traces of bismuth that might have been left. It was thought necessary for this purpose to entirely fill the abscess cavity, hence the injection was continued until the patient complained of distension. Suddenly he began to cough and brought up a quantity of olive oil through the bronchus. Three days later he returned to the office with the report that on the second day after his last treatment he could not "taste" the smell of the pus and was therefore able to eat for the first time in months with-

out vomiting. As the pus reappeard on the third day, he had returned for another olive oil injection, which was given in the same manner as before and until it produced the expectoration of olive oil. Several days of comfort followed. All other treatment was abandoned and the olive oil injections repeated every third day. After six such injections, the oil was not coughed up and the cough and expectoration stopped entirely. After three more injections of the olive oil the quantity of which was constantly diminishing in amount, the incision healed and the patient was cured as far as the pulmonary abscess was concerned. During the four weeks of treatment with olive oil he gained nine pounds in weight, and in the four months following the healing of the abscess he gained thirty pounds more.

Unfortunately the X-ray picture which was taken after the bismuth injection and which distinctly showed the communication of the bronchus with the external incision was lost. The radiograph reproduced here shows the contracted cavity representing the healed condition a year after the complete cure of the patient.

This is the first instance where I used olive oil in chest conditions, and I have used it ever since with equal success.

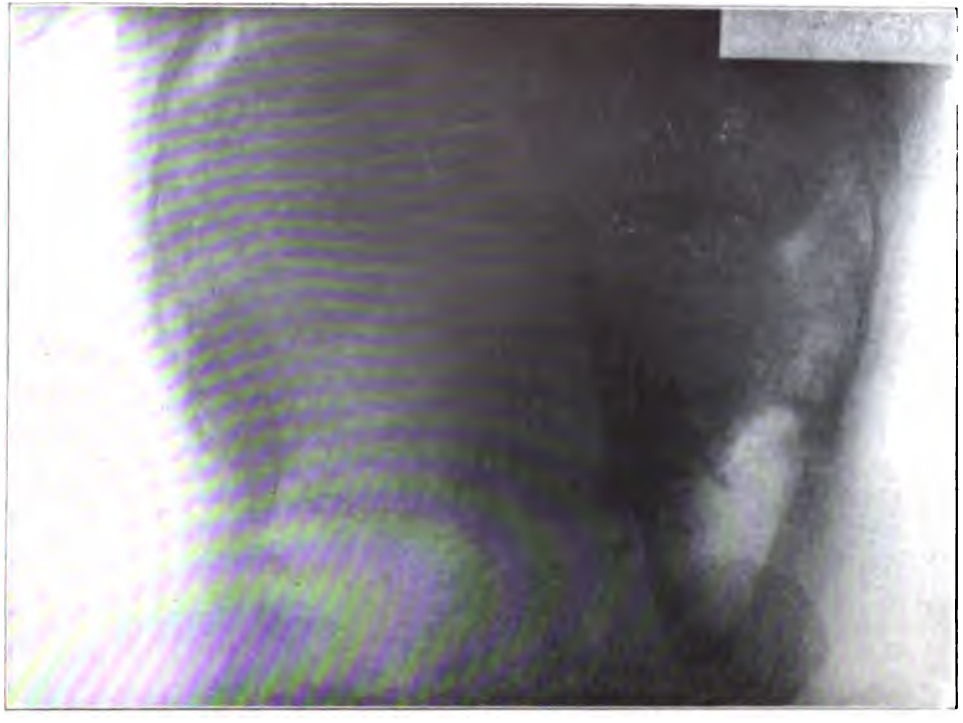

FIG. 59.—An extra-pleural abscess previously diagnosed and treated as empyema complicating pulmonary tuberculosis.

FIG. 59.

This girl, twenty-three years old, with a negative family history, had laryngeal diphtheria at the age of six, and at eleven pneumonia and pleurisy. After the attack of pleurisy she could not walk without limping and the tubercular condition of her right hip soon manifested itself. A plaster cast was applied and worn for about a year, and then replaced by a brace which she has worn ever since. Two years later, her mother noticed a protruding dorsal vertebra. A spinal brace was applied, but in spite of it pain developed in the spine, which increased in severity until four years later when it confined her to bed. A Hibb's modification of the Albie operation was performed and for about one year she was relieved. Then the pain recurred all around the body at the waist line, in the ribs and back, and finally radiated down into the left leg and she was again unable to walk. Eight months later a fistula broke open three inches to the left of the spine at the lower border of the twelfth rib, discharging a purulent matter ever since. As soon as this discharge began, the pain disappeared from the leg and she was again able to walk.

In December, 1916, she caught cold, pleuritic irritation and a constant irritating cough developed. Any attempt at speaking produced a fit of coughing and shortness of breath. Shortly after dyspnea and cyanosis developed. Since March 9, when she first began to take her temperature it ranged between 100° and 104° F. She was at this time sent to a hospital for advanced pulmonary tuberculosis, and the family were told that her condition was hopeless as the disease had extended to her lungs where it had produced a pulmonary abscess and empyema.

Four weeks previous to this writing I first saw this patient. On the earnest solicitation of her family I undertook her treatment. The above X-ray disclosed the condition to be entirely outside of the pleural cavity, the accumulation of the purulent material producing the cough and dyspnea through pressure. The pus, on examination, disclosed streptococcus and staphylococcus albus to be the principal causes of the infection. Vaccine treatment and the establishment of a counter opening near the superior border of the ileum through which bismuth paste is injected, has improved her condition by reducing her temperature to almost normal, and the amount of purulent discharge reduced to less than one-quarter of the amount formerly discharged. This improvement, together with the psychological effect brought about by the discovery that her lung was not affected, has produced a remarkable effect on her general well-being.

The many hours of tireless work which I bestowed upon the preparation of this work will not prove in vain if I have succeeded, at least in some measure, to stimulate the spread of the use of tuberculin and vaccine in the treatment of tuberculosis in general practice.

Certain it is, that the conquest of this wide-spread disease lies in the hands of the general practitioner, and it is equally certain that the final utilization of the immune response is the best weapon against this scourge.

That the signs of the times point to the awakening of the medical profession to these truths, I can give no better proof than to quote from Bandelier and Roepke, in the conclusion of their work "Tuberculin in Diagnosis and Treatment." After citing examples from many localities of the successful institution of tuberculin treatment in general practice, they conclude by saying:

"Were we to add the names of all the practitioners who, by word of mouth or in writing, have acquainted us with their reliance on tuberculin therapy, we should only tire the reader. We content ourselves with the recognition that this is the sign of a realization of what is really necessary in the fight against tuberculosis. For tuberculin will not be used to its full advantage and its far-reaching importance realized if, excluding the sanatoria, merely a few doctors make use of it. No! Tuberculin must be an integral part of the medical equipment of every physician. It must be the Alpha and Omega of our diagnosis, prophylaxis, and therapy of tuberculosis. Then it will fulfil its destiny—to assist in the extirpation of the disease. And in conclusion we may hopefully give expression to the conviction that our conception of the far-reaching importance of the specific diagnosis and therapy of tuberculosis will soon be the common property of all medical men."

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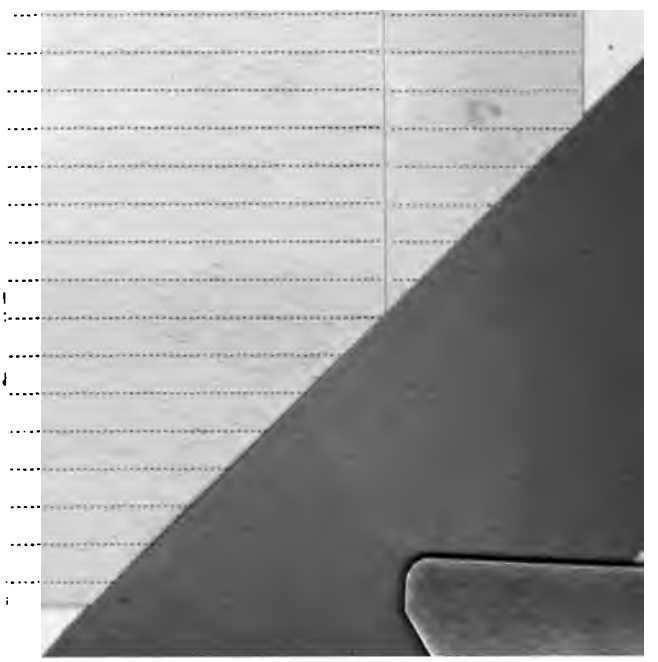
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